FINAL
STREAMLINED HUMAN HEALTH RISK ASSESSMENT
AOCs 2, 3, AND 6
NAVAL TRAINING CENTER BAINBRIDGE

Contract No. N62472-92-D-1296
Contract Task Order No. 0059

Prepared for:

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30 March 99
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AOCs 2, 3, and 6
Naval Training Center-Bainbridge

EA CTO Manager: Paul Caprio

In compliance with EA's Quality Procedures for review of deliverables outlined in the Quality Management Plan, this final deliverable has been reviewed for quality by the undersigned Senior Technical Reviewer(s). The information presented in this report/deliverable has been prepared in accordance with the approved Implementation Plan for the Contract Task Order (CTO) and reflects a proper presentation of the data and/or the conclusions drawn and/or the analyses or design completed during the conduct of the work. This statement is based upon the standards identified in the CTO and/or the standard of care existing at the time of preparation.

Senior Technical Reviewer(s)

Christine Papageorgis, Ph.D. [Date] 4/1/99

CONTENTS

CONTENTS (continued)

LIST OF FIGURES

LIST OF TABLES

LIST OF TABLES

LIST OF ACRONYMS AND ABBREVIATIONS

AOC	Area of Concern
ATSDR	Agency for Toxic Substances and Disease Registry
BBL	Blood Lead Level(s)
COPC	Constituent of Potential Concern
DDE	p,p'-Dichlorodiphenyldichloroethylene
DDD	p,p'-Dichlorodiphenyldichloroethane
DDT	p,p'-Dichlorodiphenyltrichloroethane
dL	Decaliter
EBS	Environmental Baseline Survey
EPA	Environmental Protection Agency
EPC	Exposure Point Concentration
HHRA	Human Health Risk Assessment
HI	Hazard Index
HQ	Hazard Quotient(s)
IEUBK	Integrated Exposure Uptake Biokinetic
kg	Kilogram(s)
L	Liter(s)
MDE	Maryland Department of the Environment
mg	Milligram(s)
NTC-B	Naval Training Center-Bainbridge
OAQPS	Office of Air Quality Planning and Standards
OSWER	Office of Solid Waste and Emergency Response
PAH	Polycyclic Aromatic Hydrocarbon
PRG	Preliminary Remediation Goal(s)
RBC	Risk-Based Concentration
RfD	Reference Dose(s)
RME	Reasonable Maximum Exposure

LIST OF ACRONYMS AND ABBREVIATIONS

SF	Slope Factor(s)
TCL	Target Compound List
UCLM	Upper Confidence Limit on the Mean
ug	Microgram(s)
U.S.	United States
UST	Underground Storage Tanks
VOC	Volatile Organic Compounds

EXECUTIVE SUMMARY

This document presents the results of the streamlined human health risk assessment (SHHRA) and preliminary remediation goals (PRG) calculations conducted for three Areas of Concern (AOCs) at the Naval Training Center (NTC)-Bainbridge. The SHHRA approach to risk assessment employed at these AOCs was refined to address NTC-Bainbridge exposure conditions and was agreed to by the U.S. EPA Region III and the Navy. The AOCs examined in this SHHRA were AOC 2 (Former Open Storage/Salvage Yard), AOC 3 (Former Pesticide Shop), and AOC 6 (Former Dry Cleaning Facility). Based on the current status of the site and historical activities, for the purposes for this SHHRA, future land use was conservatively assumed to be residential at each of the AOCs. PRGs were developed on the basis of the SHHRA and the potential risks identified.

AOC evaluations were conducted at NTC-Bainbridge in response to activities initiated in anticipation of transfer to the State of Maryland. Identification, sampling, analysis, and constituent of potential concern (COPC) screening was completed during the EBS Task 1 and Task 2 activities. Following regulatory review of the Pre-Final Task 2 Analytical Report (EA 1997), it was agreed that human and ecological risk assessments would be completed to further assess the risks associated with potential COPC exposures at AOCs 2, 3, and 6. This document is limited to human health risk concerns and the ecological risk assessment will be completed separately.

Sampling design at AOCs 2, 3, and 6 was proposed on the basis of previous site activity. In summary, fifteen surface soil samples were collected at AOC 2 and analyzed for metals and polycyclic aromatic hydrocarbons (PAH). Fourteen surface soil samples were collected at AOC 3 and analyzed for Target Compound List (TCL) pesticides. Ground-water samples were collected at AOC 6 and analyzed for TCL volatile organic compounds (VOC). Comprehensive AOC sampling at the NTC-Bainbridge AOCs was completed in February/March of 1997 and additional sampling at AOCs 2, 3, and 6 was completed in July of 1998.

In summary, noncancer risks were calculated for future resident adults (hazard index = 0.9) and future resident children (hazard index = 8.9) at AOC 2. Total excess cancer risks based on a 30 year exposure duration at AOC 2 was calculated to be 1 H 10^{-4}, which is the upper threshold of the acceptable cancer range (1 H 10^{-6} to 1 H 10^{-4}). Chemicals were identified as risk drivers for cancer risks exceeded 1 H 10^{-6} or non cancer risks exceeded 1.0. Chemicals identified as risk drivers at AOC 2 included: antimony, arsenic, benzo(a)anthracene, benzo(a)pyrene,

benzo(b)fluoranthene, dibenz(a,h)anthracene, indeno (1,2,3c-d)pyrene, and iron. Lead concentrations at AOC 2 were found at unacceptable levels when modeled using the Integrated Exposure Uptake Biokinetic Model (IEUBK). The IEUBK model showed an acceptable blood lead level of 6.1 :g/dL, however, the percentage of exposed children that would have a blood lead level above EPA's goal of 10 :g/dL was found to exceed the EPA's goal of 5%. The IEUBK model showed that 13.6% of the exposed children would have a blood lead level above 10 :g/dL.

At AOC 3, noncancer risks were calculated for future resident children (hazard index = 3.7) and future resident adults (hazard index = 0.3). Cancer risks were found to be 1 H 10^{-4}, which is the upper threshold for the acceptable cancer risk range (1 H 10^{-6} to 1 H 10^{-4}). Chemicals identified as risk drivers at AOC 2 included: DDD, DDE, DDT, alpha-chlordane, gamma-chlordane and heptachlor epoxide.

No unacceptable risks were found for ground-water exposures at AOC 6.

Prior to determination of PRGs for the metals at AOC2, appropriate Student T tests, were run to statistically compare metal concentrations with background metal concentrations. Based on this statistical test it was found that both arsenic and iron site concentrations were not statistically different from background at AOC 2. Although arsenic and iron at AOC 2 were not significantly different than background, the highest concentrations of these elements, located at 2-SS-6 and 2-SS-7, may represent local hot spots. However, these same stations contain the highest concentrations of the other risk drivers, thus iron and arsenic will likely be addressed at the same time the other risks are addressed.

PRGs were developed at AOCs 2, 3, and 6 in accordance with U.S. EPA guidance (1991). The goal of PRG development is to derive a concentration for each analyte that results in a reduction of COPC exposures and reduces the calculated risks to acceptable levels. For noncancer, a target hazard index of 1.0 for each target organ is considered acceptable. For cancer risks, acceptable risks range from 1 H 10^{-4} to 1 H 10^{-6} according to EPA policy (EPA 1990). Based on this range of acceptable risks, and after consultation with U.S. EPA Region III, target cancer risks were calculated for X H 10^{-6}, X H 10^{-5}, and 1 H 10^{-4}, where X is equal to the number of cancer risk drivers. Based on this methodology PRGs for AOC 2 and AOC 3 are presented in Table ES-1 and ES-2, respectively.

TABLE ES-1 SUMMARY OF PRGs AT AOC 2

COPC	Cancer or Noncancer COPC[(1)]	Range of Cancer PRGs (mg/kg)	Noncancer PRGs (mg/kg)	Blood Lead Level PRG (mg/kg)
Antimony			27.5	
Benzo(a)anthracene	C	0.9 – 17.5		
Benzo(a)pyrene	C	0.09 – 7.1		
Benzo(b)fluoranthene	C	0.9 – 17.5		
Dibenz(a,h) anthracene	C	0.09 –1.8		
Indeno(1,2,3) pyrene	C	0.9 – 17.5		
Lead				350

(1) Carcinogenic COPCs will be represented by a "C."

* Represents a concentration less than, or within the range, of background concentrations.

TABLE ES-2 SUMMARY OF PRGs AT AOC 3

COPC	Cancer or Noncancer COPC [(1)]	Range of Cancer PRGs (mg/kg)	Noncancer PRGs (mg/kg)
DDD	C	2.3 – 38.3	
DDE	C	1.6 – 27.0	
DDT	C	1.6 – 27.0	4.3
Alpha Chlordane	C	1.6 – 25.8	4.1
Gamma Chlordane	C	1.6 – 25.8	4.1
Heptachlor Epoxide	C	0.05 – 0.8	0.4

(1) Carcinogenic COPCs will be represented by a "C."

1. INTRODUCTION

This Streamlined Human Health Risk Assessment (HHRA) was prepared by EA Engineering, Science, and Technology, Inc. (EA) under contract No. N62472-92-D-1296, Contract Task Order No. 0059, and Contract Modification No. 0014. The SSHRA approach was discussed and agreed upon by U.S. EPA Region III (EPA) and the Navy. A copy of the risk assessment scope of work is provided in Appendix C. The HHRA was completed for three areas of concern (AOCs) at the former Naval Training Center-Bainbridge (NTC-B): AOC 2, AOC 3, and AOC 6 (Figure 1-1).

AOC evaluations for NTC-B began as part of the Environmental Baseline Survey (EBS) activities initiated in response to Base Realignment and Closure Plans for the NTC-B facility. EA completed Task 1 of the EBS in March 1996. Work completed under Task 1 included a visual site inspection, interviews, records review, and preparation of a "Position Paper" (EPA 1995), a document prepared by U.S. EPA Region III in consultation with the Maryland Department of the Environment (MDE). This document outlined existing environmental concerns at NTC-B that warranted additional investigation. Based on the results of the Task 1 activities, and in accordance with the Position Paper, a scope of work for Task 2 (sample collection and analysis) of the EBS AOCs at NTC-B was prepared.

Ten AOCs were identified for the Task 2 evaluations and surface soil, sediment, and ground- and surface water samples were collected in February and March of 1997. The1997 samples were analyzed, and screened for constituents of potential concern (COPC) using U.S. EPA Region III Risk Based Concentrations (RBCs) for residential exposures. The screening results were presented in the *Pre-Final Task 2 Analytical Report* (EA 1997). Screening level exceedances were reported in the pre-final report and three AOCs were scoped for additional field sampling, and human health and ecological risk characterizations. This report presents the results of the human health risk assessment completed for AOCs 2, 3, and 6. The ecological risk characterizations will be completed and delivered under separate cover. Complete discussions of the field sampling efforts and laboratory analyses, and relevant background information will be final Task 2 report.

1.1 SITE DESCRIPTION AND ACTIVITIES

The former NTC-B is situated on approximately 1,250 acres in Cecil County, Maryland, just to the east of the town of Port Deposit. NTC-B is currently inactive with respect to Naval

operations. NTC-B was constructed in 1941 as a training center for World War II Navy recruits. The facility was partially deactivated after World War II, but experienced major activity following the Korean crisis in 1951. In the post-war years, NTC-B became the host for various schools and functions, including the Naval Preparatory School, the Nuclear Power School, the Naval Reserve Manpower Center, WAVES Headquarters, and a U.S. Naval Hospital. Operations at NTC-B were reduced in 1972, and NTC-B was formally closed in 1976; however, the Navy has retained ownership.

Since the closure in 1976, various activities have occurred at NTC-B including the sponsorship of a Job Corps Center by the Department of Labor from 1978 until 1990, a structure demolition project, various contractor operations, and the use of some portions of NTC-B by the Cecil County Community College Truck Driver Training School.

1.2 AOC 2: COAL STORAGE AREAS AND OPEN SALVAGE/STORAGE YARD DESCRIPTION AND BACKGROUND

AOC 2 consists of two discreet locations, the Open Salvage/Storage Yard (AOC 2a) and the Coal Storage Areas (AOC 2b) shown in Figures 1-2 and 1-3. Coal ash/cinders were used as paving material in the Open Salvage/Storage Yard (AOC 2a) where scrap metal was stored. In addition, coal storage operations at the coal storage pile (AOC 2b) were formerly conducted at NTC-B when the facility was active. The long-term presence of coal and coal ash/cinders in these areas was identified during the EBS Task 1 investigation. This area was identified as an AOC due to the potential presence of elevated metals and/or polycyclic aromatic hydrocarbon (PAH) concentrations in surrounding soil.

The concern regarding the former Open Salvage/Storage Yard and the former Coal Storage Area is associated with the potential for metals and/or PAH to have been released into surrounding soil as a result of the long-term storage of coal, scrap metal, or ash and cinders in these areas. The collection of surface soil samples and analyses for PAH and metals in the vicinity of these areas was used to evaluate the presence/absence of elevated concentrations of COPC in soil at this AOC. The results of the COPC evaluation were used to identify and characterize potential risks associated with onsite human exposures.

A total of thirteen surface soil samples were collected at the Open Salvage/Storage Yard (AOC 2a) and two samples were taken at the Coal Storage Area (AOC 2b), during the two Task 2 field

sampling events (Figures 1-2 and 1-3). The analytical results from the two sampling events at AOC 2a and AOC 2b were combined for the purposes of completing the SHHRA. The combined data set from the AOC 2a and AOC 2b will be identified as AOC 2 for the remainder of the report. Table 1-1 presents the samples collected from AOC 2 and the associated analytical metals and PAH data.

1.3 AOC 3: PESTICIDE SHOP DESCRIPTION AND BACKGROUND

The former pesticide shop, identified as an area where pesticide storage, formulation, and distribution activities took place when NTC-B was active, was identified as an AOC due to the potential presence of elevated pesticide concentrations in the surrounding soil. Consequently, it was included in the Task 2 field sampling effort.

Fourteen surface soil samples were collected in the vicinity of the former pesticide shop and submitted for laboratory analysis of Target Compound List (TCL) pesticides Figure 1-4. Table 1-2 summarizes the samples collected and analytical results.

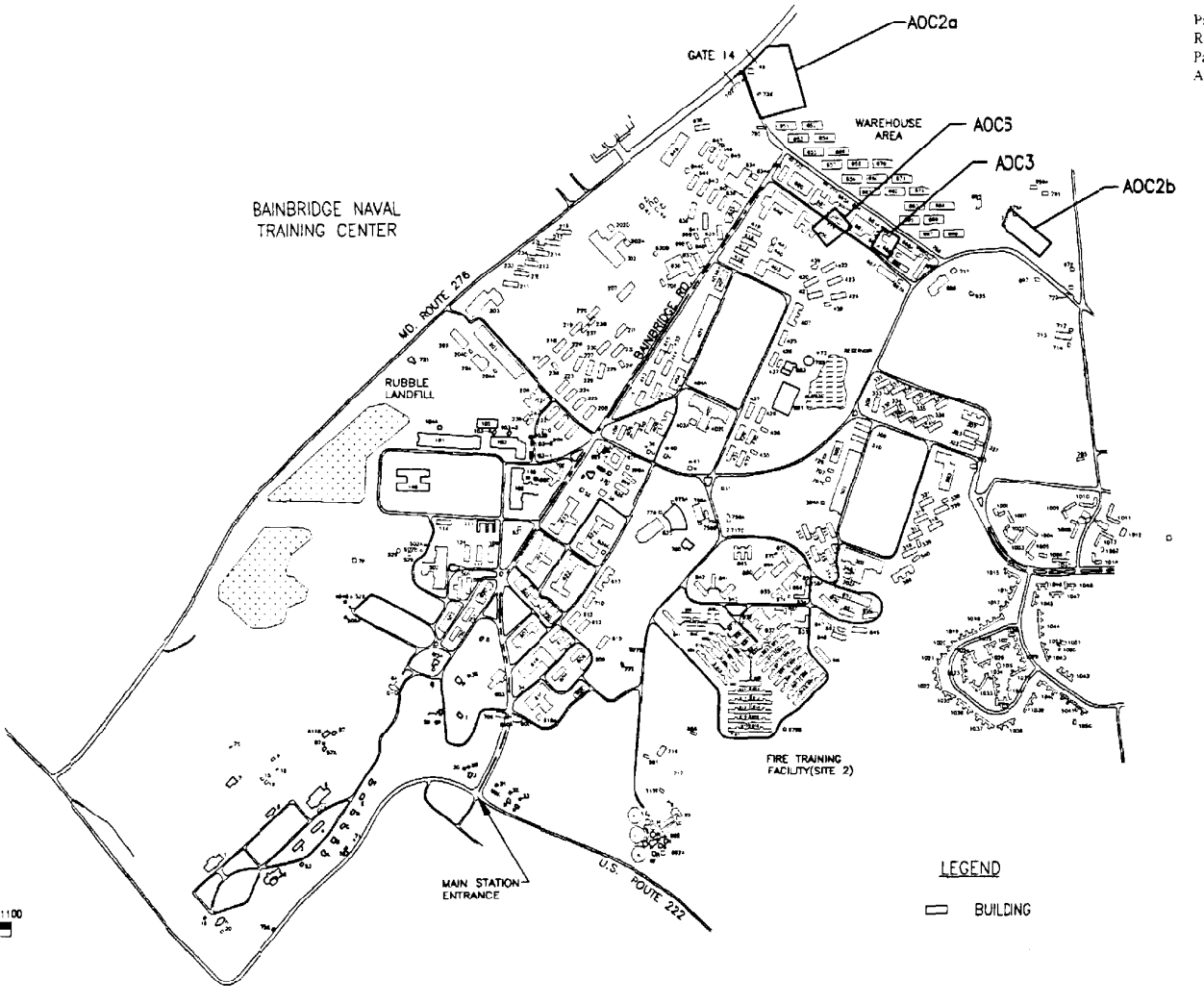
1.4 AOC 6: FORMER DRY CLEANING FACILITY DESCRIPTION AND BACKGROUND

The dry cleaning facility for NTC-B was located at former Building 718. While active, underground storage tanks (USTs) were used at the site to store dry-cleaning. During UST removal, evidence of leakage from the tanks was observed by MDE, and one ground-water monitoring well was installed to assess the presence of volatile organic compound (VOC) concentrations in ground water.

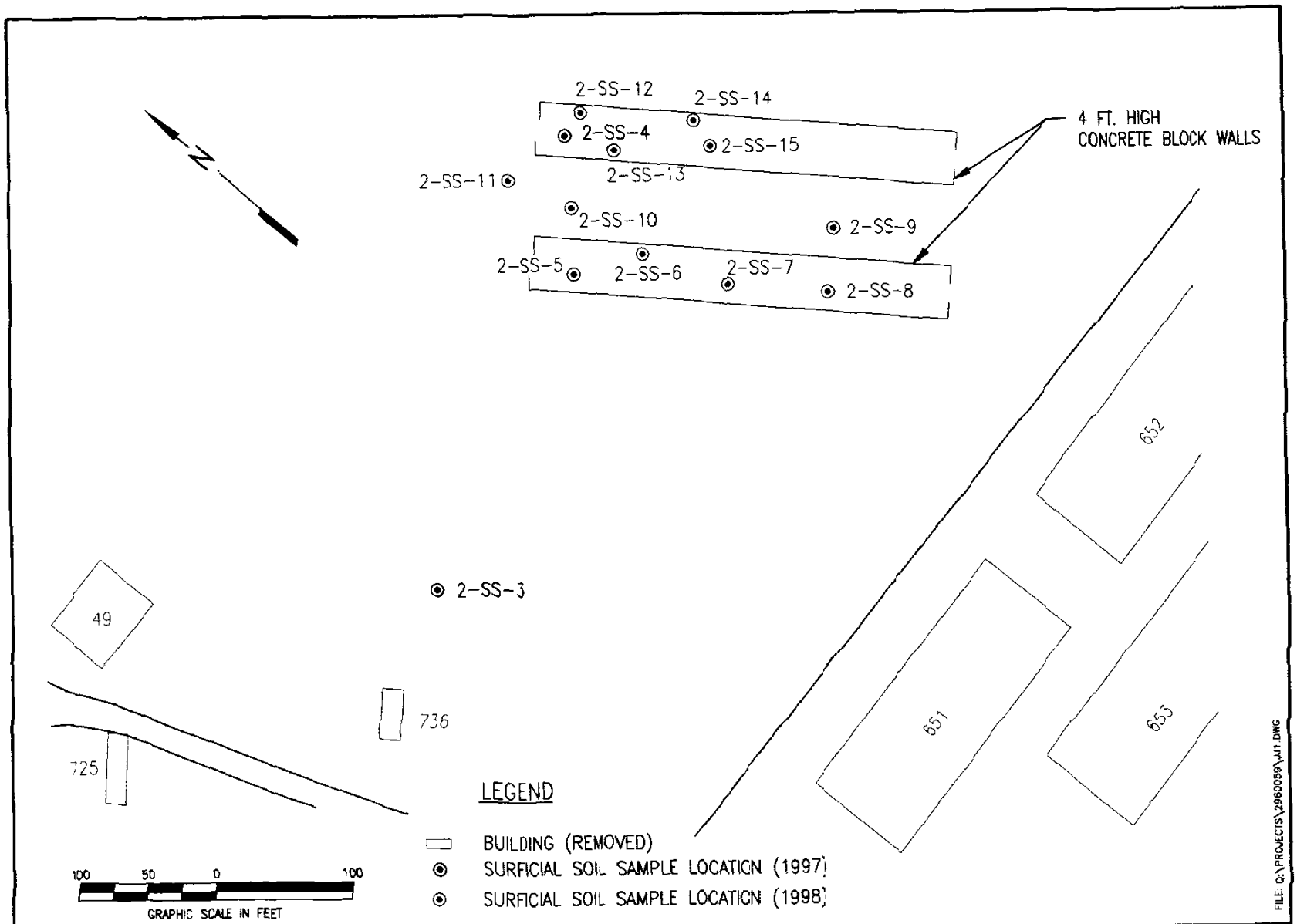
Two ground-water samples (including one field and one duplicate quality control sample) were collected from the AOC 6 monitoring well during the first EBS Task 2 sampling event (conducted in February/March 1997). No screening criteria exceedances were identified in the AOC ground-water sample (6-GW-1). However, trichloroethene and 1,2-dibromo-3-chloropropane were reported at, and slightly above screening criteria in the field duplicate sample (6-GW-2) (Table 1-3). Due to the inconsistent analytical results reported during the first Task 2 sampling event, an additional ground-water sample was collected from the well during the second Task 2 sampling event (conducted in July 1998) and analyzed for VOC. No VOC were detected in the July 1998 sample, which was consistent with the original field sample collected in

February/March 1997. The ground-water analytical results from both Task 2 sampling events (including the field duplicate) are summarized in Table 1-3. The human health

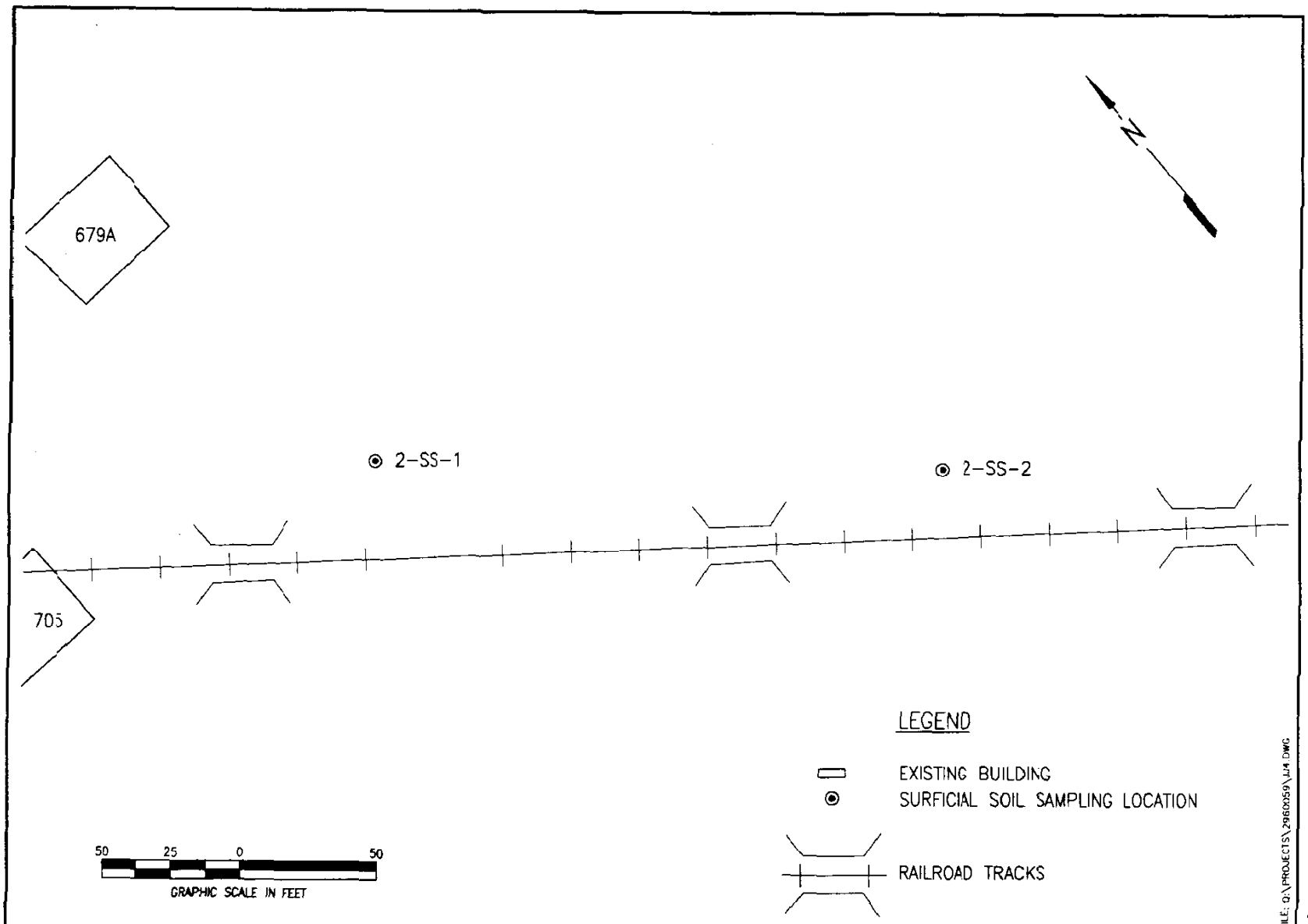
Assessment presented in the following report however, was based on the July 1998 analytical results.



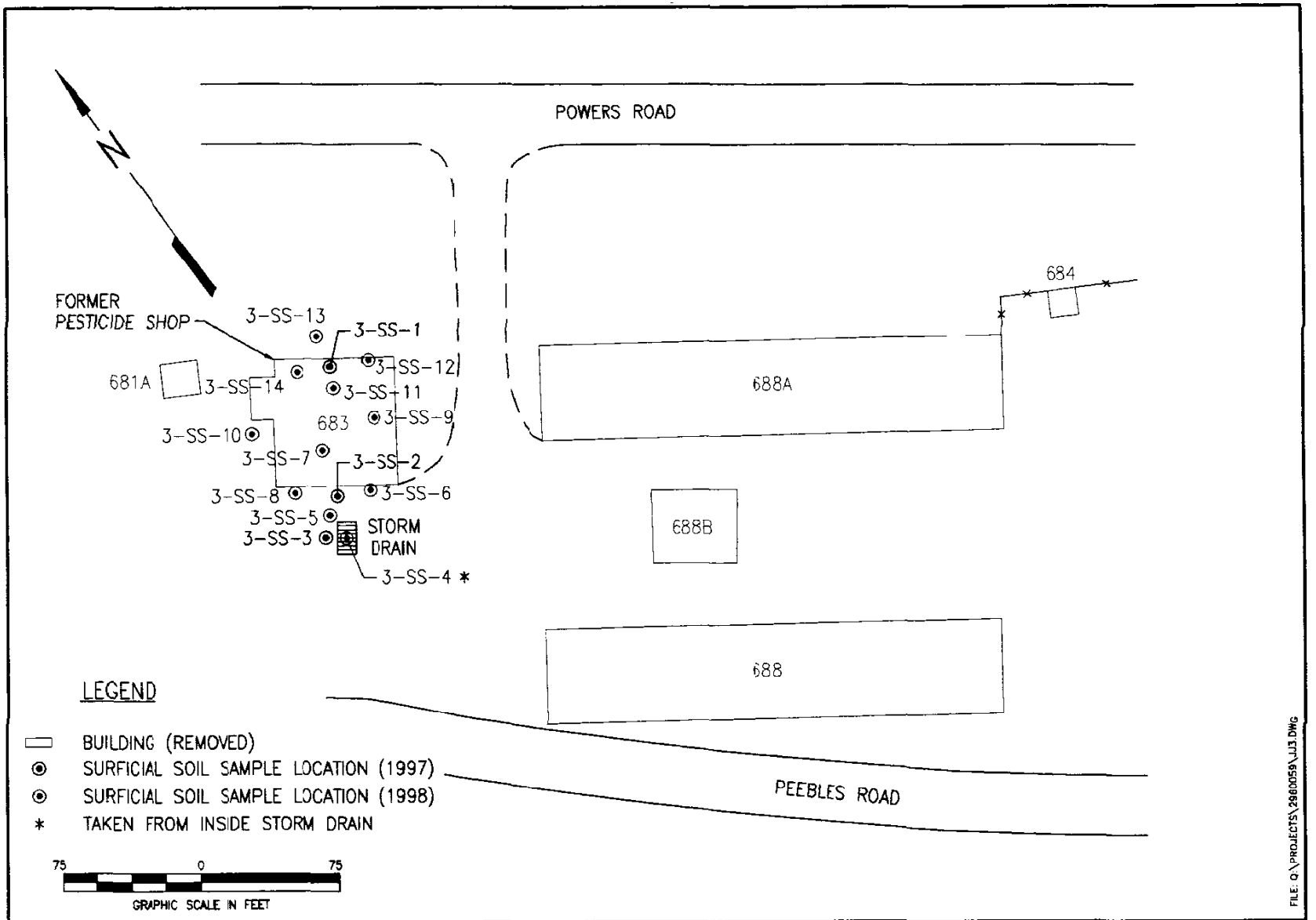
EA ENGINEERING, SCIENCE, AND TECHNOLOGY	NAVAL TRAINING CENTER, BAINBRIDGE PORT DEPOSIT, MARYLAND	SITE LOCATIONS FOR AOC2, AOC3, AND AOC6	DESIGNED BY: TC	DRAWN BY: PMH	DATE: 3-26-99	PROJECT NO.: 296.0059	FILE NAME: JJBASE
			CHECKED BY: JBJ	PROJECT MGR.: JPC	SCALE: 1" = 1100'	DRAWING NO.: -	FIGURE: 1-1



EA ENGINEERING, SCIENCE, AND TECHNOLOGY	NAVAL TRAINING CENTER, BAINBRIDGE PORT DEPOSIT, MARYLAND	SAMPLE LOCATIONS 2-SS-3 THROUGH 2-SS-15 FOR AOC-2a FORMER OPEN STORAGE/SALVAGE AREA	DESIGNED BY TC	DRAWN BY JBS	DATE 3-26-99	PROJECT NO. 296.0059
			CHECKED BY JBJ	PROJECT MGR. JPC	SCALE 1"=100'	FIGURE 1-2



EA ENGINEERING, SCIENCE, AND TECHNOLOGY	NAVAL TRAINING CENTER, BAINBRIDGE PORT DEPOSIT, MARYLAND	SAMPLE LOCATIONS 2-SS-1 AND 2-SS-2 FOR AOC-2b FORMER COAL STORAGE AREA	DESIGNED BY TC	DRAWN BY PMH	DATE 3-25-99	PROJECT NO. 296.0059
			CHECKED BY JBJ	PROJECT MGR. JPC	SCALE 1"=50'	FIGURE 1-3



EA ENGINEERING, SCIENCE, AND TECHNOLOGY	NAVAL TRAINING CENTER, BAINBRIDGE PORT DEPOSIT, MARYLAND	SAMPLE LOCATIONS FOR AOC-3 FORMER PESTICIDE SHOP	DESIGNED BY TC	DRAWN BY JBS	DATE 3-26-99	PROJECT NO. 296.0059
			CHECKED BY JBJ	PROJECT MGR. JPC	SCALE 1"=75'	FIGURE 1-4

TABLE 1-1 ANALYTICAL DATA SUMMARY FOR AOC 2

Analytes	Screening Value (a)	Former Coal Storage Area AOC 2b		Former Open Storage Salvage Area AOC 2a												
		2-SS-1	2-SS-2	2-SS-3	2-SS-4	2-SS-5	2-SS-6	2-SS-7	2-SS-8	2-SS-9	2-SS-10	2-SS-11	2-SS-12	2-SS-13	2-SS-14	2-SS-15
Metals (mg/kg)																
ALUMINUM	**7800**	**9370**	6860	7340	5390	4050 *	**44400** *	**57900** *	4200 *	2440 *	3950 *	4650 *	**11400** *	4790 *	3430 *	2720 *
ANTIMONY	**3.1**	0.19 UL	0.18 UL	**0.84** J	**6.7** L	**3.2** J	**17.8** J	**71** J	1.8 J	1 B	2 J	1.4 J	1.2 J	1.9 J	**4.6** J	**3.9** J
ARSENIC	**0.43(b)**	**3.4**	**2.5**	**5.9**	**17.7**	**9.6** L	**32.3** L	**74** L	**2.5** L	**15.1** L	**16.2** L	**14.7** L	**4.8** L	**3.9** L	**12.2** L	**4.2** L
BARIUM	**550**	50 *	21.4 *	66.7 *	175 *	99.6	**759**	514	53.9	87.6	64.7	81.1	53.4	46.2	125	65.3
BERYLLIUM		0.43 B	0.36 B	0.33 B	0.28 B	0.32 J	3.4 J	3.0 J	0.26 J	0.33 J	0.3 J	0.37 J	0.43 J	0.37 J	0.42 J	0.16 J
CADMIUM	**3.9**	0.25 U	0.23 U	0.37 U	**13.3**	2.4	**8.1**	**10.9**	0.31 J	0.52 J	1	0.44 J	2.4	**6**	**16.1**	**6.5**
CALCIUM		46700 J	884 J	1830 *	9850 J	1270	18900	10200	1210	3760	1040	3750	1110	672	2970	1820
CHROMIUM	**39**	12.9 *	13.7 *	11.4 *	36.1 *	15.4 J	**114** J	**148** J	8 J	5.5 J	11.6 J	11.9 J	19.7 J	12.2 J	22.9 J	18.6 J
COBALT		6.1	5.3	7.1	9	4.9 J	68.4	42.6 J	4.4 J	2 J	6.2	3.1 J	6.9	6.2	9.2	7
COPPER		12.6	11.8	38.7	203	37.1 J	309 J	197 J	17.9 J	14.6 J	242 J	24.5 J	14.1 J	42.1 J	118 J	61.9 J
IRON	**2300**	**19000**	**11900**	**11100**	**45800**	**16600** *	**175000** *	**117000** *	**10500** *	**5870** *	**12100** *	**12700** *	**22500** *	**10100** *	**29200** *	**11800** *
LEAD	**400**	52.1 J	27.9 J	74.9 J	**903** J	181	**3950**	**1150**	54.6	60.8	133	67.1	44.5	136	**545**	**550**
MAGNESIUM	**160**	**4250**	**1680**	**735**	**4510**	**738**	**5030** J	**15400**	**523** J	**566** J	**468** J	**534** J	**1110**	**472** J	**494** J	**526** J
MANGANESE	**2.3**	**340** *	**235** *	**363** *	**446** *	**226** L	**3710** L	**879** L	**253** L	**53.7** L	**307** L	**180** L	**152** L	**151** L	**1030** L	**54.8** L
MERCURY		0.05	0.02 B	0.44	7	0.4 K	0.58 UN	4.1 K	0.06 UN	0.21 K	0.16 K	0.22 K	0.19 K	2.9 K	1.5 K	0.57 K
NICKEL		10.3	8.8	20.5	80.6	11.7	104	118	5.1	9.5	6.2	8.4	11.2	20.6	26	12.3
POTASSIUM		750	830	445	640	212 J	2520 J	2700 J	234 J	183 J	211 J	187 J	371 J	171 J	300 J	149 J
SELENIUM		0.26 B	0.224	1.6	1.4 B	3.3 L	13 L	8.5 L	0.91 B	1.4 L	0.87 B	1.4 L	1.5 L	1.1 B	2.9 L	1.3 B
SILVER		0.45 U	0.42 U	1.5 B	0.9 B	0.11 U	1.2 U	2.8 J	0.11 U	0.12 U	0.1 U	0.12 U	0.12 U	0.11 U	0.49 J	0.11 U
SODIUM		60.9 B	21 B	57.3 B	113 B	98.4 J	869 J	836 J	92.3 J	159 J	77.5 J	196 J	98 J	106 J	147 J	90.4 J
THALLIUM		0.46 B	0.34 U	0.54	0.69 U	0.46 L	1.2 UL	1.1 UL	0.11 UL	0.12 UL	0.11 UL	0.12 UL	0.24 L	0.11 UL	0.12 UL	0.1 UL
VANADIUM	**55**	19.3	15.9	19.5	**106**	21.2	**200**	**245**	24.9	12.4	20.9	21.4	44.5	19	18	24
ZINC	**2300**	43.9	34.9	147	1430	286 J	1990 J	**2760** J	105 J	180 J	158 J	166 J	149 J	450 J	**2760** J	1190 J
PAH (ug/kg)																
ACENAPHTHENE		2400 U	210 U	360 U	4400 U	170 J	79	19000 J	410	1700 J	1000	1900 J	1000	590	3500 J	25000J J
ACENAPHTHYLENE		4700 U	400 U	690 U	8500 U	82 U	84 U	83 U	130	85 U	77 U	88 U	84 U	81 U	86 U	79 U
ANTHRACENE		770	21 U	36U U	740	10 J	6 U	2000 J	23	140 J	100	130 J	75	51	230 J	2700 J
BENZ[A]ANTHRACENE	**870(b)**	**1600**	30	76	**1900**	110 J	20	**5000** J	110	370 J	220	390 J	280	110	790 J	**4800** J
BENZO[A]PYRENE	**87(b)**	**1800** L	70 L	**190** L	**2400** L	**280** J	30	**4300** J	**96**	**440** J	**240**	**480** J	**310** E	**150**	**940** J	**4300** J
BENZO[B]FLUORANTHENE	**870(b)**	**1800**	66	190	**1900**	570 J	45	5600 J	130	510 J	290	570 J	370	180	**1200** J	**5300** J
BENZO[GHI]PERYLENE		790	51	94	1200	1200 J	75	3300 J	170	320 J	180	380 J	210	110	770 J	3100 J
BENZO[K]FLUORANTHENE		1100	33	85	1300	240 J	14	2500 J	46	220 J	120	230 J	150	78	500 J	2300 J
CHRYSENE		1900	53 L	110	2600	120 J	17	3800 J	85	210 J	180	270 J	180	86	630 J	3300 J
DIBENZ[A,H]ANTHRACENE	**87(b)**	**470** U	40 U	69 U	**850** U	**100** J	4.6	450 J	14	42 J	32	50 J	32	16	93 J	**370** J
FLUORANTHENE		3600	48	210	4500	110 J	47	12000 J	200	1000 J	500	1100 J	560	300	1900 J	370 J
FLUORENE		470 U	40 U	69 U	850 U	8.2 U	8.4 U	800 J	8.1 U	56 J	37	41 J	13	23	45 J	370 J
INDENO[1,2,3-CD]PYRENE	**870(b)**	750	38	130	**960**	670 J	40	**1900** J	65	180 J	93	180 J	120	62	360 J	370 J
NAPHTHALENE		2400 U	210 UL	360 U	4400 U	47 U	48 U	320 J	47 U	370 J	70	630 J	74	91	340 J	370 J
PHENANTHRENE		3200	25	130	4200	41 J	36	7100 J	110	790 J	380 E	870 J	290	250	1200 J	370 J
PYRENE		3100	43	150	3700	81	36	8600 J	160	820 J	400 E	840 J	480 E	240	1400 J	370 J

Bold indicates exceeds Screening Value
(a) Screening value from October 1998 Region III RBC Table
(b) Carcinogens
Non cancer values are 1/10th the concentrations found on the RBC table

J = Estimated value
U = Not detected
L = Reported value may be biased low
* = Duplicate analysis outside control limit
K = Reported value may be biased high
B = Between IDL and CRDL
N = MS outside of control limits
E = Outside of calibration range

TABLE 1-2 ANALYTICAL DATA SUMMARY FOR AOC 3

Pesticides (ug/kg)	Screening Value [1]	3-SS-1	3-SS-2	3-SS-3	3-SS-4	3-SS-5	3-SS-6	3-SS-7	3-SS-8	3-SS-9	3-SS-10	3-SS-11	3-SS-12	3-SS-13	3-SS-14
4,4'-DDD	**2700***	**7500** J	1100 J	580 J	210 J	920 J	1400 J	1700 J	2800 J	290 J	7300 J	1300 J	**19000** J	**56000** J	**13000** J
4,4'-DDE	**1900***	**3200**	760	1500	900	1400	1400	1700	1600	350	**3900**	1200	**9200**	**22000** J	**7500**
4,4'-DDT	**1900***	**14000**	**5200**	**2500**	950	**6000**	**7000**	**7900**	**6400**	890	**11000**	**3700**	**28000**	**110000**	**34000**
ALDRIN		940 U	390 U	200 U	79 U	190 U	390 U	390 UJ	390 U	29 U	380 U	190 U	940 U	9700 U	1900 U
ALPHA-BHC		940 U	390 U	200 U	79 U	190 U	390 U	390 U	390 U	29 U	380 U	190 U	940 U	9700 U	1900 U
ALPHA-CHLORDANE	**1800***	1400	240	80	64 J	190 U	390 U	1700 J	390 U	42 J	840 J	220 J	**2300** J	**15000** J	**2400** J
BETA-BHC		940 U	390 U	200 U	79 U	190 U	390 U	390 U	390 U	29 U	380 U	190 U	940 U	9700 U	1900 U
CHLORDANE		16000	3900 U	2000 U	790 U	1900 U	3900 U	14000	3900 U	360 J	6500 J	1900 U	19000	150000	19000 U
DELTA-BHC		940 U	390 U	200 U	79 U	190 U	390 U	390 U	390 U	29 U	380 U	190 U	940 U	9700 U	1900 U
DIELDRIN		1800 U	760 U	400 U	160 U	380 U	780 U	780 U	780 U	57 U	760 U	370 U	1900 U	19000 U	3900 U
ENDOSULFAN I		940 U	390 U	200 U	79 U	190 U	390 U	390 U	390 U	29 U	380 U	190 U	940 U	9700 U	1900 U
ENDOSULFAN II		1800 U	760 U	400 U	160 U	380 U	780 U	780 U	780 U	57 U	760 U	370 U	1900 U	19000 U	3900 U
ENDOSULFAN SULFATE		1800 UJ	760 UJ	400 UJ	160 U	380 U	780 U	780 U	780 U	57 U	760 U	370 U	1900 U	19000 U	3900 U
ENDRIN		1800 U	760 U	400 U	160 U	380 U	780 U	780 U	780 U	57 U	760 U	370 U	1900 U	19000 U	3900 U
ENDRIN ALDEHYDE		1800 U	760 U	400 U	160 U	380 U	780 U	780 U	780 U	57 U	760 U	370 U	1900 U	19000 U	3900 U
ENDRIN KETONE		1800 U	760 U	400 U	160 U	380 U	780 U	780 U	780 U	57 U	760 U	370 U	1900 U	19000 U	3900 U
GAMMA-BHC		940 U	390 U	200 U	79 U	190 U	390 U	390 U	390 U	29 U	380 U	190 U	940 U	9700 U	1900 U
GAMMA-CHLORDANE	**1800***	1600	230 J	97 J	47	200 J	390 U	**2200**	390 U	57	1100	290	**3000**	**17000** J	**2900**
HEPTACHLOR		940 U	390 U	200 U	79 UJ	190 UJ	390 UJ	390 U	390 UJ	29 UJ	380 UJ	190 UJ	940 UJ	9700 UJ	1900 UJ
HEPTACHLOR EPOXIDE	**70***	940 U	390 U	200 U	**130**	**230** J	**630**	**600** J	390 U	53	**650** J	190 U	940 U	9700 U	1900 U
METHOXYCHLOR		9400 U	3900 U	2000 U	790 U	1900 U	3900 U	3900 U	3900 U	290 U	3800 U	1900 U	9400 U	97000 U	19000 U
TOXAPHENE		18000 U	7600 U	4000 U	7900 U	19000 U	39000 U	39000 U	39000 U	2900 U	38000 U	19000 U	94000 U	970000 U	190000 U
SOLIDS-TOTAL RESIDUE (TS)		90.00	86.00	86.00											
CARBON, TOTAL ORGANIC (mg/Kg)					20000 J	37200	54400	19700	21800	15700	26400	13400	9310	51800	29600

Bold indicates exceeds Screening Value
(1) Screening value from October 1998 Region III RBC Table. Carcinogens are denoted by an *
Non cancer values are 1/10th the concentrations found on the RBC table,

J = Estimated value
U = undetected

TABLE 1-3 GROUND-WATER ANALYTICAL DATA SUMMARY FOR AOC 6

Volatiles (ug/L)	**6-GW-1 Feb-97**	**6-GW-1 (DUP) Feb-97**	**6-GW-1 Jul-98**
1,1,1,2-TETRACHLOROETHANE	1 U	1 U	1 U
1,1,1-TRICHLOROETHANE	1 U	0.5 J	1 U
1,1,2,2-TETRACHLOROETHANE	1 U	1 U	1 U
1,1,2-TRICHLOROETHANE	1 U	1 U	1 U
1,1-DICHLOROETHANE	1 U	1 U	1 U
1,1-DICHLOROETHENE	1 U	1 U	1 U
1,1-DICHLOROPROPENE	1 U	1 U	1 U
1,2,3-TRICHLOROBENZENE	1 U	1	1 U
1,2,3-TRICHLOROPROPANE	1 U	1 U	1 UJ
1,2,4-TRICHLOROBENZENE	1 U	1 U	1 U
1,2,4-TRIMETHYLBENZENE	1 U	0.6 J	1 U
1,2-DIBROMO-3-CHLOROPROPANE	1 U	1 K	1 U
1,2-DIBROMOETHANE	1 U	1 U	1 U
1,2-DICHLOROBENZENE	1 U	1 U	1 U
1,2-DICHLOROETHANE	1 U	1 U	1 U
1,2-DICHLOROPROPANE	1 U	1 U	1 U
1,3,5-TRIMETHYLBENZENE	1 U	1 U	1 U
1,3-DICHLOROBENZENE	1 U	1 U	1 U
1,3-DICHLOROPROPANE	1 U	1 U	1 U
1,4-DICHLOROBENZENE	1 U	1 U	1 U
2,2-DICHLOROPROPANE	1 U	1 U	1 U
2-CHLOROTOLUENE	1 U	1 U	1 U
4-CHLOROTOLUENE	1 U	1 U	1 U
BENZENE	1 U	1 U	1 U
BROMOBENZENE	1 U	1 U	1 U
BROMOCHLOROMETHANE	1 U	1 U	1 U
BROMODICHLOROMETHANE	1 U	1 U	1 U
BROMOFORM	1 U	1 U	1 U
BROMOMETHANE	2 U	2 U	1 U
CARBON TETRACHLORIDE	1 U	1 U	1 U
CHLOROBENZENE	1 U	1 U	1 U
CHLOROETHANE	2 U	2 U	1 U
CHLOROFORM	1 U	1 U	1 U
CHLOROMETHANE	2 UL	2 UL	1 U
CIS-1,2-DICHLOROETHENE	1 U	1 U	1 U
DIBROMOCHLOROMETHANE	1 U	1 U	1 U
DIBROMOMETHANE	1 U	1 U	1 U
DICHLORODIFLUOROMETHANE	2 R	2 R	1 U
ETHYLBENZENE	1 U	1 U	1 U
HEXACHLOROBUTADIENE	1 U	1 U	1 U
ISOPROPYLBENZENE	1 U	1 U	1 U
METHYLENE CHLORIDE	1 U	0.6 B	1 UJ
M-XYLENE AND P-XYLENE	1 U	1 U	1 U
NAPHTHALENE	1 U	2 K	1 U

Volatiles (ug/L)	6-GW-1 Feb-97	6-GW-1 (DUP) Feb-97	6-GW-1 Jul-98
N-BUTYLBENZENE	1 U	1 U	1 U
N-PROPYLBENZENE	1 U	1 U	1 U
O-XYLENE	1 U	1 U	1 U
P-ISOPROPYLTOLUENE	1 U	1 U	1 U
SEC-BUTYLBENZENE	1 U	1 U	1 U
STYRENE	1 U	1 U	1 U
TERT-BUTYLBENZENE	1 U	1 U	1 U
TETRACHLOROETHENE	1 U	0.8 J	1 U
TOLUENE	1 U	1 U	1 U
TRANS-1,2-DICHLOROETHENE	1 U	1 U	1 U
TRICHLOROETHENE	1 U	5	1 U
TRICHLOROFLUOROMETHANE	2 U	2 U	1 U
VINYL CHLORIDE	2 UL	2 U	1 U

U = Undetected
J = Reported value may not be accurate or precise
K = Reported value may be biased high
R = Unreliable result (rejected)

2. OVERVIEW OF HUMAN HEALTH RISK ASSESSMENT PROCESS

The purpose of human health risk assessment is to identify and characterize potential risks associated with human exposure to site-related constituents of potential concern (COPCs) in order to support (1) informed decision-making and (2) remedial response activities resulting in regulatory compliance decisions. The objective of the assessment reported in this section was to conduct a streamlined human health risk assessment for EBS AOCs 2, 3, and 6: Former Coal Storage Area/Former Storage Salvage Yard, Former Pesticide Shop, and Former Dry Cleaning Facility, respectively.

In accordance with guidance from the U.S. Environmental Protection Agency (EPA) Region III and consensus with the Navy, the risk assessment associated with AOCs 2, 3, and 6 is presented in a more abbreviated and modified format than that which would be used for a more comprehensive baseline risk assessment. Hence, the designation of this report as a "streamlined" human health risk assessment.

Given the historical activities and the current status of the site, future land use for this streamlined human health risk assessment was assumed to be residential land use for AOCs 2, 3, and 6.

Within the context of this report the following procedures were performed:

X All site-related soil data for each of the three AOCs were evaluated and processed in accordance with standard EPA guidance for data evaluation (EPA 1989); *Section 3.0 Screening and Selection of Constituents of Potential Concern (COPCs)*;

X COPCs were selected at all AOCs via comparison to appropriate EPA Region III Risk-Based Concentrations (RBCs) (EPA 1998) in conjunction with a limited number of additional considerations, and comparisons of inorganic analytes and PAHs to appropriate background concentrations; *Section 3.0 Screening and Selection of COPCs*;

X Receptor populations considered were children and adults in a future residential land use scenario; the exposure pathway evaluated quantitatively was in accordance with *Section 4.0 Exposure Assessment and Considerations*;

- Toxicity values were established using EPA general guidance (EPA 1989) as well as EPA Region III guidance (EPA 1998); *Section 5.0 Toxicity Assessment*; and

X Risks were characterized and presented for both noncancer and cancer endpoints, in accordance with EPA guidance (EPA 1989), and accompanying uncertainties were briefly described; *Section 6.0 and Section 7.0 Risk Characterization and Uncertainties*.

Primary information, such as 95% UCLMs, selection of COPCs, toxicity values, and summary risks, are included in the report to illustrate critical information pertaining to each of the AOCs. Accompanying appendices are provided to serve as detailed information for each component of the risk assessment (i.e., exposure equations and parameters, chemical-specific noncancer and cancer intakes and risks, and chemical-specific toxicity information).

manganese, mercury, vanadium, and zinc) and five PAHs (benzo[a]anthracene, benzo[a]pyrene, benzo[b]fluoranthene, dibenz[a,h]anthracene, and indeno[1,2,3-cd]pyrene) failed screening and were carried forward as COPCs in surface soil.

AOC 3, Former Pesticide Shop, had six pesticides which failed screening (4,4'-DDD, 4,4'-DDE, 4,4'-DDT, α-chlordane, γ-chlordane, and heptachlor epoxide) and were retained as COPCs in surface soil.

Ground Water COPCs

No ground-water COPCs were identified at AOC 6.

A summary list of the identified COPCs at each of the AOCs are listed in Table 3-3.

TABLE 3-1
OCCURRENCE, DISTRIBUTION AND SELECTION OF CHEMICALS OF POTENTIAL CONCERN
AOC 2, DRMO SALVAGE YARD, NTC BAINBRIDGE, MARYLAND

Scenario Timeframe:	Future
Medium:	Soil
Exposure Medium:	Surface Soil
Exposure Point:	Surface Soil at AOC 2

CAS Number	Chemical	Min. Conc.	Min. Qual.	Max. Conc.	Max. Qual.	Units	Location of Maximum Conc.	Detection Frequency	Range of Detection Limits	Conc. Used for Screening	Background Value [1]	Screening Toxicity Value[2]	COPC Flag	(3) Rationale for Contaminant Deletion or Selection
7429-90-5	ALUMINUM	2440	*	57900	*	MG/KG	2-SS-7	15/15	1.50-16.2	57900	14506	7800	**Yes**	ASL
7440-36-0	ANTIMONY	0.84	J	71	J	MG/KG	2-SS-7	13/15	0.21-2.30	71	0.25	3.1	**Yes**	ASL
7440-38-2	ARSENIC	2.5	L	74	L	MG/KG	2-SS-7	15/15	0.21-2.30	74	8.8	0.43 C	**Yes**	ASL
7440-39-3	BARIUM	21.4	*	759		MG/KG	2-SS-6	15/15	0.73-8.1	759	140	550	**Yes**	ASL
7440-41-7	BERYLLIUM	0.16	J	3.4	J	MG/KG	2-SS-6	15/15	0.100-1.20	3.4	0.7	16		BSL
7440-43-9	CADMIUM	0.31	J	16.1		MG/KG	2-SS-14	12/15	0.100-1.20	16.1	0.43	3.9	**Yes**	ASL
7440-70-2	CALCIUM	672		46700	J	MG/KG	2-SS-1	15/15	2.20-24.3	46700	21500	0		NUT
7440-47-3	CHROMIUM	5.5	J	148	J	MG/KG	2-SS-7	15/15	0.31-3.50	148	15.6	23	**Yes**	ASL
7440-48-4	COBALT	2	J	68.4		MG/KG	2-SS-6	15/15	0.63-6.9	68.4	6.5	470		BSL
7440-50-8	COPPER	11.8		309	J	MG/KG	2-SS-6	15/15	0.42-4.60	309	21.5	310		BSL
7439-89-6	IRON	5870	*	175000	*	MG/KG	2-SS-6	15/15	13.6-150.	175000	19212	2300	**Yes**	ASL
7439-92-1	LEAD	27.9	J	3950		MG/KG	2-SS-6	15/15	0.100-0.120	3950	10000	400	**Yes**	ASL
7439-95-4	MAGNESIUM	468	J	15400		MG/KG	2-SS-7	15/15	3.50-38.2	15400	2911	0		NUT
7439-96-5	MANGANESE	53.7	L	3710	L	MG/KG	2-SS-6	15/15	0.100-1.20	3710	764	160	**Yes**	ASL
7439-97-6	MERCURY	0.02	B	7		MG/KG	2-SS-4	13/15	0.050-0.59	7	0.4	2.3	**Yes**	ASL
7440-02-0	NICKEL	5.1		118		MG/KG	2-SS-7	15/15	1.00-11.6	118	8.7	160		BSL

CAS Number	Chemical	Min. Conc.	Min. Qual.	Max. Conc.	Max. Qual.	Units	Location of Maximum Conc.	Detection Frequency	Range of Detection Limits	Conc. Used for Screening	Background Value (1)	Screening Toxicity Value(2)	COPC Flag	Rationale for (3) Contaminant Deletion or Selection
7440-09-7	POTASSIUM	149	J	2700	J	MG/KG	2-SS-7	15/15	8.8-97.2	2700	1128	0		NUT
7782-49-2	SELENIUM	0.26	B	13	L	MG/KG	2-SS-6	14/15	0.21-2.30	13	1.1	39		BSL
7440-22-4	SILVER	0.49	J	2.8	J	MG/KG	2-SS-7	4/15	0.100-1.20	2.8	0.27	39		BSL
7440-23-5	SODIUM	21	B	869	J	MG/KG	2-SS-6	15/15	2.90-32.4	869	50.5	0		NUT
7440-28-0	THALLIUM	0.24	L	0.46	L	MG/KG	2-SS-5	3/15	0.100-1.20	0.46	0.36	0.6		BSL
7440-62-2	VANADIUM	12.4		245		MG/KG	2-SS-7	15/15	0.31-3.50	245	38.6	55	**Yes**	ASL
7440-66-6	ZINC	34.9		2760	J	MG/KG	2-SS-7	15/15	0.73-8.1	2760	63.9	2300	**Yes**	ASL
83-32-9	ACENAPHTHENE	79		25000	J	UG/KG	2-SS-15	11/15	44.0-49.0	25000		470000		BSL
208-96-8	ACENAPHTHYLENE	130		130		UG/KG	2-SS-8	1/15	77.0-86.0	130		230000		BSL
120-12-7	ANTHRACENE	10	J	2700	J	UG/KG	2-SS-15	12/15	5.5-6.0	2700		2300000		BSL
56-55-3	BENZ[A]ANTHRACENE	20		5000	J	UG/KG	2-SS-7	15/15	2.20-2.50	5000		870 C	**Yes**	ASL
50-32-8	BENZO[A]PYRENE	30		4300	J	UG/KG	2-SS-7	15/15	2.20-2.50	4300		87 C	**Yes**	ASL
205-99-2	BENZO[B]FLUORANTHENE	45		5600	J	UG/KG	2-SS-7	15/15	2.20-2.50	5600		870 C	**Yes**	ASL
191-24-2	BENZO[GHI]PERYLENE	51		3300	J	UG/KG	2-SS-7	15/15	2.20-2.50	3300		230000		BSL
207-08-9	BENZO[K]FLUORANTHENE	14		2500	J	UG/KG	2-SS-7	15/15	2.20-2.50	2500		8700 C		BSL
218-01-9	CHRYSENE	17		3800	J	UG/KG	2-SS-7	15/15	5.5-6.0	3800		87000 C		BSL
53-70-3	DIBENZ[A,H]ANTHRACENE	4.6		450	J	UG/KG	2-SS-7	11/15	2.20-2.50	450		87 C	**Yes**	ASL
206-44-0	FLUORANTHENE	47		14000	J	UG/KG	2-SS-15	15/15	7.7-8.6	14000		310000		BSL
86-73-7	FLUORENE	13		1900	J	UG/KG	2-SS-15	8/15	7.7-8.6	1900		310000		BSL
193-39-5	INDENO[1,2,3-CD]PYRENE	38		1900	J	UG/KG	2-SS-7	15/15	2.20-2.50	1900		870 C	**Yes**	ASL
91-20-3	NAPHTHALENE	70		1300	J	UG/KG	2-SS-15	8/15	44.0-49.0	1300		160000		BSL
85-01-8	PHENANTHRENE	25		14000	J	UG/KG	2-SS-15	15/15	5.5-6.0	14000		230000		BSL
129-00-0	PYRENE	36		10000	J	UG/KG	2-SS-15	15/15	9.9-11.0	10000		230000		BSL

Definitions: N/A = Not Available
SQL = Sample Quantitation Limit
COPC = Chemical of Potential Concern
ARAR/TBC = Applicable or Relevant and Appropriate Requirement/To Be Considered
MCL = Federal Maximum Contaminant Level
SMCL = Secondary Maximum Contaminant Level
C = Carcinogenic
N = Non-Carcinogenic

(1) Background values derived from statistical analysis (EA 1997).

(2) RBC Region III, October 1998.

(3) Rationale codes Selection Reasons:
- Infrequent Detection but Associated Historically (HIST)
- Frequent Detection (FD)
- Toxicity Information Available (TX)
- Above Screening Levels (ASL)

Deletion Reason:
- Infrequent Detection (IFD)
- Background Levels (BKG)
- No Toxicity Information (NTX)
- Essential Nutrient (NUT)
- Below Screening Level (BSL)

(4) Lead action level from EPA OSWER Directive #9355.4-12

J = Estimated
L = Reported value may be biased low
B = Between IDL and CRDL
* = Duplicate analysis outside control limits

TABLE 3-2
OCCURRENCE, DISTRIBUTION AND SELECTION OF CHEMICALS OF POTENTIAL CONCERN
AOC 3, FORMER PESTICIDE SHOP, NTC BAINBRIDGE, MARYLAND

Scenario Timeframe:	Future
Medium:	Soil
Exposure Medium:	Surface Soil
Exposure Point:	Surface Soil at AOC 3

CAS Number	Chemical	Minimum Concentration	Minimum Qualifier	Maximum Concentration	Maximum Qualifier	Units	Location of Maximum Concentration	Detection Frequency	Range of Detection Limits	Concentration Used for Screening	(1) Background Value	(2) Screening Toxicity Value	COPC Flag	(3) Rationale for Contaminant Deletion or Selection
72-54-8	4,4'-DDD	210	J	56000	J	UG/KG	3-SS-13	14/14	57.0-19000	56000		2700 C	**Yes**	ASL
72-55-9	4,4'-DDE	350		22000	J	UG/KG	3-SS-13	14/14	57.0-19000	22000		1900 C	**Yes**	ASL
50-29-3	4,4'-DDT	890		110000		UG/KG	3-SS-13	14/14	57.0-19000	110000		1900 C	**Yes**	ASL
5103-71-9	ALPHA-CHLORDANE	42	J	15000	J	UG/KG	3-SS-13	11/14	29.0-9700	15000		1800 C	**Yes**	ASL
5103-74-2	GAMMA-CHLORDANE	47		17000	J	UG/KG	3-SS-13	12/14	29.0-9700	17000		1800 C	**Yes**	ASL
1024-57-3	HEPTACHLOR EPOXIDE	53		650	J	UG/KG	3-SS-10	6/14	29.0-9700	650		70 C	**Yes**	ASL

Definitions:
N/A = Not Applicable
SQL = Sample Quantitation Limit
COPC = Chemical of Potential Concern
ARAR/TBC = Applicable or Relevant and Appropriate Requirement/To Be Considered
MCL = Federal Maximum Contaminant Level
SMCL = Secondary Maximum Contaminant Level
J = Estimated Value
C = Carcinogenic
N = Non-Carcinogenic

(1) No background values gathered.

(2) RBC Region III, October 1998.

(3) Rationale codes Selection Reason Infrequent Detection but Associated Historically (HIST)
Frequent Detection (FD)
Toxicity Information Available (TX)
Above Screening Levels (ASL)
Deletion Reason: Infrequent Detection (IFD)
Background Levels (BKG)
No Toxicity Information (NTX)
Essential Nutrient (NUT)
Below Screening Level (BSL)

TABLE 3-3 FINAL LIST OF COPCs FOR EBS AOCs 2 AND 3

COPC	Surface Soil
AOC 2	
Inorganics	
Aluminum	X
Antimony	X
Arsenic	X
Barium	X
Cadmium	X
Chromium	X
Iron	X
Lead	X
Manganese	X
Mercury	X
Vanadium	X
Zinc	X
PAHs	
Benzo(a)anthracene	X
Benzo(a)pyrene	X
Benzo(b)fluoranthene	X
Dibenz(a,h)anthracene	X
Indeno(1,2,3,c-d)pyrene	X
Naphthalene	X
AOC 3	
Pesticides	
DDD	X
DDE	X
DDT	X
Alpha-Chlordane	X
Gamma-Chlordane	X
Heptachlor Epoxide	X

4. EXPOSURE ASSESSMENT

The purpose of an exposure assessment is to determine the populations that potentially may be exposed to site-related chemicals, the pathways by which exposures may occur, and the magnitude, frequency, and duration of these potential human exposures. The exposure assessment focuses on the COPCs present at each of the AOCs.

Estimating Exposure Point Concentrations

The first step in this process is transforming the data by taking the natural logarithm of the data set should it be a lognormal distribution. Otherwise, the untransformed data are used. To determine if the data needs to be transformed, the data set is examined using the Shapiro Wilkes test to determine the distribution of the data set. The data set for both AOCs was determined to be lognormal ($\forall$=0.05) and, therefore, the transformed data was used to determine the 95th percentile upper confidence limit on the mean (95% UCLM). In cases where the 95% UCLM exceeded the maximum detected concentration, the maximum detected concentration was used. The 95% UCLMs were estimated using the equation given below (USEPA 1992).

The transformed data were then used in the following equation:

$$95\ UCLM = e^{(\bar{x} + 0.5s^2 + sH/\sqrt{n-1})}$$

Where:

95% UCML	=	95th percentile upper confidence limit on the mean
e	=	Constant (base of the natural logarithm, equal to 2.718)
$\overline{x}$	=	Mean of the transformed data
s	=	Standard deviation of the transformed data
H	=	H-Statistic
n	=	Number of samples in the data set

Summary statistics for COPCs in surface soil at the two AOCs are listed in Tables 4-1 and 4-2.

Exposure Population and Pathways

Under a future residential land use scenario for all AOCs, two maximally exposed receptor populations were identified as being the primary populations of concern for this streamlined risk assessment: future adult residents and future child residents. The medium evaluated as the exposure source was surface soil. Residential adults are exposed to COPCs in surface soil for long periods of time (up to 24 years), while residential children are exposed to COPCs in surface soil for a period of 6 years. Both populations are exposed at a frequency of 350 days/year. The primary exposure pathways which were evaluated quantitatively for both receptor populations at each of the AOCs are:

X *Ingestion of surface soil by residential adults and children; and*
X *Dermal contact with surface soil by residential adults and children.*

Ground water was not a specific medium of concern since no COPCs were identified; therefore, this medium does not provide an exposure point for this human health risk assessment.

The reasonable maximum exposure (RME) is intended to represent the highest exposure that is reasonable expected to occur at the site. A variety of EPA guidance and reference documents were used for:

- Assumed values for exposure parameters,
- Descriptions of exposure parameter values used for quantifying exposure for individual exposure pathways for each receptor group, and
- Algorithms for calculating (lifetime) average daily doses.

These values are tabulated in Appendix A, Table A-1.

Exposures Associated with Lead in Soil

Exposures, and subsequently health risks, for receptors exposed to lead in soil are estimated in the context of Blood Lead Levels (BLLs). Determination of risk due to lead cannot be quantified using the risk assessment procedures invoked for all the COPCs as described in the preceding sections, because (1) the unique behavior of lead in the human body, (2) inadequate or limited

knowledge about its toxicity, and (3) the corresponding inability to assign reliable toxicity values. Lead has been classified by the U.S. EPA as a probable human carcinogen (category B2) based on sufficient evidence in rats developing renal tumors from lifetime ingestion of lead, although evidence in humans is inadequate (U.S. EPA 1994). Currently, lead is not regulated as a carcinogen because it appears to be more potent as a toxicant to the hemopoietic system by inhibiting heme synthesis. The basis for lead toxicity is its ability to bind to ligating groups in physiologically critical biomolecules, which may then disrupt their function by competing with essential metal ions for binding sites, inhibiting enzyme activity, and altering ion transport (Calabrese and Kenyon 1991). In the absence of detailed information on lead by which to ascribe RfDs, noncarcinogenic risks to lead are quantitatively estimated by using pharmacokinetic models or qualitatively assessed by comparison to best-judgement action levels proposed by the EPA Office of Solid Waste and Emergency Response (OSWER).

Initially, the range and representative concentrations of lead in soil were compared to the U.S. EPA screening level of 400 mg/kg for lead in residential soils. If this level was exceeded, the U.S. EPA Integrated Exposure Uptake Biokinetic (IEUBK) model was used to assess residential childhood exposure to lead. The blood lead level of 10 µg/dL has been identified as being associated with several adverse toxic effects in humans, specifically, elevated blood pressure in adult male humans, and developmental effects such as toxicity to the fetus following maternal exposure (ATSDR 1993c). In addition to an assigned blood lead level of 10 ug/dL, EPA has a goal that no more than 5% of the exposed children should exceed the 10 ug/dL blood lead level. Two endpoints are employed in this risk assessment as a comparative estimate of the blood level above which toxic effects may be evidenced in children:

- Blood lead levels should not exceed 10 µg/dL and
- No more than 5% of the exposed children can exceed the 10 µg/dL level.

The IEUBK Model is used to estimate blood lead concentrations resulting from exposure to environmental sources. This method has been suggested by the U.S. EPA Office of Air Quality Planning and Standards (OAQPS) Staff Report (U.S. EPA 1989). The IEUBK Model is a three-stage method for estimating total blood lead levels. First, the intake of lead from each source is assessed. Second, the uptake of lead from each source is determined. Finally, the relationship between the uptake of lead and blood lead concentration is applied.

The U.S. EPA has created a software program of the IEUBK Model, considered "state-of-the-art" for predicting blood lead levels in children ages 0-84 months, for use on a personal computer.

The most current software is LEAD version 0.99D ("LEAD99D"). LEAD99D is used in this assessment for estimating blood lead levels in children at AOC 2. The model output is a probability distribution function describing the percentage of children predicted to have blood levels exceeding 10 µg/dL. More specific information on this model is contained in U.S. EPA (1994).

Lead was detected in surface soil at AOC 2 and was greater than the screening level of 400 mg/kg. For AOC 2, the mean lead concentration was 3,950 mg/kg. The LEAD99D was run for this surface soil concentration. The results are discussed in Section 5.1, Risk Characterization for Lead. For additional toxicity information about lead, see Appendix B.

TABLE 4-1 SUMMARY STATISTICS FOR COPCs AT AOC 2, FORMER COAL STORAGE AREA AND FORMER OPEN SALVAGE YARD

COPC	Frequency Detected	Range of Detected Concentrations	Arithmetic Mean	95% UCL on the Mean
SURFACE SOIL (mg/kg)				
Aluminum	15/15	2,440-57,900	8.12	19,635
Antimony	13/15	0.84-71	0.71	54.3
Arsenic	15/15	2.5-74	2.19	29.5
Barium	15/15	21-759	4.51	264
Cadmium	12/15	0.31-16.1	0.44	53.2*
Chromium	15/15	5.5-148	2.93	52.3
Iron	15/15	5,870-175,000	34,078	60,150
Lead	15/15	27.9-3,950	528	1,969
Manganese	15/15	53.7-3,710	5.67	1,199
Mercury	13/15	0.02-7	1.02	9.8*
Vanadium	15/15	12.4-245	3.46	94
Zinc	15/15	34.9-2,760	5.8	3,625*
PAH				
Benzo(a)anthracene	15/15	0.020-5	0.006	8.2*
Benzo(a)pyrene	15/15	0.030-4.3	0.006	5.3*
Benzo(b)fluoranthene	15/15	0.045-5.6	0.004	5.7*
Dibenz(a,h)anthracene	11/15	0.005-0.45	0.005	0.5*
Indeno(1,2,3-c,d)pyrene	15/15	0.038-1.9	0.005	1.8
Naphthalene	8/15	0.070-1.3	0.005	2.4*

Notes: * Indicates that the constituent's maximum detected concentration was used in risk calculations because the 95% UCML exceeded the maximum detected value.

TABLE 4-2 SUMMARY STATISTICS FOR COPCs AT AOC 3, FORMER PESTICIDE SHOP

COPC	Frequency Detected	Range of Detected Concentrations	Arithmetic Mean	95% UCL on the Mean
SURFACE SOIL (mg/kg)				
Pesticides				
DDD	14/14	0.210-56	0.008	53
DDE	14/14	0.350-22	0.008	9.6
DDT	14/14	0.890-110	0.009	59.3
Alpha-chlordane	11/14	0.042-15	0.006	13.2
Gamma-chlordane	12/14	0.047-17	0.006	17.2*
Heptachlor Epoxide	6/14	0.053-0.65	0.006	1.7*

Notes: * Indicates that the constituent's maximum detected concentration was used in risk calculations because the 95% UCML exceeded the maximum detected value.

5. TOXICITY ASSESSMENT

Toxicity values were obtained for all final COPCs. Values which were sought for noncancer endpoints encompassed chronic and subchronic oral reference doses (RfDs). Chronic and subchronic dermal RfDs were developed, as needed, from their corresponding oral RfDs.

Cancer toxicity values included oral slope factors (SFs). Dermal SFs were developed by adjusting oral SFs. More detailed information on the toxicity values used for assessing risks is provided in the two tables of cancer and noncancer toxicity values (Tables 5.1 and 5.2).

Summaries of in-depth toxicity information for the final COPCs are provided in Appendix B.

TABLE 5-1 TOXICITY VALUE (SLOPE FACTORS) FOR POTENTIAL CARCINOGENIC EFFECTS VIA ORAL AND DERMAL EXPOSURE ROUTES

Analyte	Cancer Slope Factor			
	Oral [1] $(mg/kg\text{-}day)^{-1}$	Weight of Evidence [1]	Tumor Type [1]	Dermal $(mg/kg\text{-}day)^{-1}$ (Dermal adjustment factor and source)
INORGANICS				
Aluminum	NA	NA	NA	NA
Antimony	NA	NA	NA	NA
Arsenic	1.5	A	Skin	1.5 (95%, NCEA 1992)
Barium	NA	NA	NA	NA
Cadmium	NA	NA	NA	NA
Chromium	NA	D	NA	NA
Lead	NA	B2	NA	NA
Manganese	NA	NA	NA	NA
Mercury	NA	D	NA	NA
Vanadium (surrogate: vanadium pentoxide)	NA	NA	NA	NA
Zinc	NA	D	NA	NA
SEMIVOLATILE PESTICIDES				
DDD	0.24	B2	Liver	0.24
DDE	0.34	B2	Hepatocellular carcinomas, hepatomas	0.34 (100%, ATSDR 1993a)

Analyte	Cancer Slope Factor			
	Oral [1] $(mg/kg\text{-}day)^{-1}$	Weight of Evidence [1]	Tumor Type [1]	Dermal $(mg/kgs\text{-}day)^{-1}$ (Dermal adjustment factor and source)
DDT	0.34	B2	Liver, benign and malignant	0.34 (100%, ATSDR 1993a)
alpha-Chlordane	0.35	B2	Hepatocellular carcinoma	0.4 (80% ATSDR 1994)
gamma-Chlordane	0.35	B2	Hepatocellular carcinoma	0.4 (80% ATSDR 1994)
VOLATILE PESTICIDE				
Heptachlor epoxide	9.1	B2	Hepatocellular carcinoma	11.4
PAHs				
Benzo(a)anthracene	0.73 [2]	B2	Forestomach papillomas, pulmonary adenomas, hepatomas	NA
Benzo(a)pyrene	7.3	B2	Forestomach, squamous cell papillomas and carcinomas	NA
Benzo(b)fluoranthene	0.73 [2]	B2	NA [3]	NA
Dibenzo(a,h)anthracene	7.3 [2]	B2	Pulmonary adenomas and carcinomas, mammary carcinomas, and hemangio-endotheliomas	NA

NA = Toxicity value or other information not available or is not a known carcinogen.
Cancer classifications for weight of evidence:
A = Human carcinogen
B2 = Probable human carcinogen (sufficient evidence in animals, inadequate to no evidence in humans)
C = Possible human carcinogen (inadequate data in humans, limited evidence in animals)
D = Not classifiable (inadequate evidence in humans and animals)
(1) Information obtained from IRIS (USEPA 1998) unless otherwise noted.
(2) Slope factor was developed by adjusting the oral SF for benzo(a)pyrene, using USEPA toxicity equivalence factors for each compound (USEPA 1996).
(4) IRIS cancer classification was not based on oral data, but consistency of effect was found among other routes (USEPA 1998).

TABLE 5-2 SUBCHRONIC AND CHRONIC TOXICITY VALUES (REFERENCE DOSES) FOR POTENTIAL NONCARCINOGENIC EFFECTS VIA ORAL AND DERMAL EXPOSURE ROUTES

Analyte	Reference Doses [1]					
	Oral RfD (mg/kg-day)	Confidence Level	Critical Effect	UF/MF	Dermal (mg/kg-day)	Dermal (Adjustment Factor Source)
INORGANICS						
Aluminum	1.0 [2]	NA	Developmental Neurotoxicity	NA	0.2	0.2
Antimony	0.0004	Low	Increased mortality, altered blood glucose and cholesterol	1000/1	0.00004	0.00004 (10% ATSDR 1992)
Arsenic	0.0003	Medium	Skin hyperpig-mentation; keratosis; vascular effects	3/1	0.0003	0.0003 (95% NCEA 1992)
Barium	0.07	Medium	Hypertension; increased kidney weight	3/1	0.07	0.07 (100% NCEA 1993)
Cadmium	0.001	High	Significant proteinuria	10/1	0.000025	0.00025 (2.5% IRIS)
Chromium	0.003	Low	Renal effects	300/3	0.00003	0.00003 (1% ATSDR, 1993b)
Iron	0.3		Blood, liver, and gastrointestinal system		0.3	NA
Lead	NA					
Manganese	0.02	Medium	Central nervous system effects	1/3	0.02	0.02
Mercury (Inorganic mercury)	0.0001	High	Immune System	1000/1	0.0001	0.0003
Vanadium (surrogate: vanadium pentoxide)	0.007 [3]	Low	NA	100/1	0.0001	0.0001 (2% ATSDR 1992)

Analyte	Reference Doses [1]					
	Oral RfD (mg/kg-day)	Confidence Level	Critical Effect	UF/MF	Dermal (mg/kg-day)	Dermal (Adjustment Factor Source)
Zinc	0.3	Medium	Significant decrease in erythrocyte superoxide dismutase in adult human females	3/1	0.06	0.25
SEMIVOLATILE PESTICIDES						
DDD	NA	NA	NA	NA	NA	NA
DDE	NA	NA	NA	NA	NA	NA
DDT	0.0005	Medium	Liver lesions	100/1	0.0005	0.0005
alpha-Chlordane	0.0005	Medium	Hepatic necrosis	300/1	0.0004	0.0005
gamma-Chlordane	0.0005	Medium	Hepatic necrosis	300/1	0.0004	0.0005
VOLATILE PESTICIDE						
Heptachlor epoxide	0.000013	Low	Increased liver-to-body weight ratio	1000/1	0.00001	NA
PAHs						
Benzo(a)anthracene	NA	NA	NA	NA	NA	NA
Benzo(a)pyrene	NA	NA	NA	NA	NA	NA
Benzo(b)fluoranthene	NA	NA	NA	NA	NA	NA
Dibenz[a,h]anthracene	NA	NA	NA	NA	NA	NA
Indeno(1,2,3-c,d)-pyrene	NA	NA	NA	NA	NA	NA

UF/MF = Uncertainty Factor/ Modifying Factor
NA = Not available or not applicable.

[1] Information was obtained from IRIS (USEPA 1998) unless otherwise indicated.
[2] Provisional value was obtained from USEPA/NCEA (1998). Dermal RfD value is based on the provisional USEPA/NCEA (1998) oral value.

6. RISK CHARACTERIZATION

The human health risk assessment for AOCs 2 and 3 evaluated potential onsite human exposure to COPCs for the following receptor populations:

X Future adult residents
X Future child residents

The potential risks to future residents at AOCs 2 and 3 are discussed individually in the following sections.

6.1 CANCER AND NONCANCER RISKS ASSOCIATED WITH AOC 2 – FORMER COAL STORAGE AREA/ FORMER OPEN SALVAGE YARD

Residential Children

Chronic hazard indices for health effects other than cancer were estimated for child residents exposed to COPCs in surface soil via incidental ingestion and dermal contact with surface soil using specific exposure parameters. The total noncancer risk for children was greater than 1 under RME conditions with a HI of 8.8 (Table 6-1). HIs driving risks for future residential children were mainly due to the exposure to antimony (2.0), arsenic (1.3), and iron (2.6), mainly through incidental ingestion of surface soil. The target organ for antimony, the critical effect on which the antimony RfD is based, is the hematopoietic system or blood. The target organ/system for arsenic is the skin and for iron the target organ/system is blood, liver and gastrointestinal tract. Table 6-2 shows the individual HQs for each COPC and exposure route.

Excess lifetime cancer risks associated with chronic exposure to surface soil were 1 $H10^{-4}$ under RME conditions (Table 6-3). These risks within the acceptable range of 1 $H10^{-4}$ to 1 $H10^{-6}$ according to EPA policy (EPA 1990). The COPCs that contributed to the excess risk were arsenic (5 H 10^{-5}) and benzo(a)pyrene (3 H 10^{-5}), via the incidental ingestion of soil. Table 6-4 shows the risks due to individual COPC and exposure route.

Risk Characterization for Lead

The LEAD99D (U.S. EPA 1994) program was used to estimate hypothetical child blood lead levels. The mean lead concentration found in surface soil at AOC 2 was entered into the

multisource dust model. Other than the surface soil lead concentration, standard default values (70% soil to dust contribution) were utilized in the model runs. Based on LEAD99D model outputs, children exposed to lead in surface soil, under the hypothetical residential exposure scenario would be expected to have mean blood lead levels of:

X 6.1 µg/dL, with approximately 13.64% of the exposed children's blood lead levels above the level of concern at AOC 2 (see Figure 6-1).

The predicted mean blood lead levels for children residing at AOC 2 are below the 10 µg/dL Alevel of concern." Although blood lead levels are below the 10 µg/dL recommended BLL concentration, 13.64% of the exposed children will have a BLL greater than the EPA recommended 10 µg/dL (See Figure 6-1). EPA recommends that no more than 5% of the exposed children will have a blood lead level above the 10 µg/dL. It can be assumed that children exposed to AOC 2 surface soil will experience elevated blood lead levels.

Adult Residents

Chronic hazard indices for health effects other than cancer were estimated for adult residents exposed to COPCs in surface soil via incidental ingestion using specific exposure parameters and dermal contact with surface soil by approximating ingestion risks. The total noncancer risk for adults was less than 1 under RME conditions, a hazard index (HI) of 0.9 (Table 6-1).

Excess lifetime cancer risks associated with chronic exposure to surface soil were 4 $H10^{-5}$ under RME conditions (Table 6-3). These risks fall within the acceptable range of 1 $H10^{-4}$ to 1 $H10^{-6}$ according to EPA policy (EPA 1990). There are no excess cancer health concerns for adult residents at the AOC 2. However, the combined cancer risks for residential adults and children assuming an exposure duration of 30 years is 1 $H10^{-4}$.

6.2 CANCER AND NONCANCER RISKS ASSOCIATED WITH AOC 3 - FORMER PESTICIDE SHOP

Residential Children

Chronic hazard indices for health effects other than cancer were estimated for child residents exposed to COPCs in surface soil via incidental ingestion and dermal contact with surface soil using specific exposure parameters. The total noncancer risk for children was greater than 1 under RME conditions, a HI of 3.7 (Table 6-1). HIs greater than 1 for future residential children were driven mainly from exposure to DDT a HQ of 1.8. The target organ for DDT toxicity is the liver. Table 6-5 lists individual HQs for each COPC and exposure route.

Excess lifetime cancer risks associated with chronic exposure to surface soil were 7 $H10^{-5}$ under RME conditions (Table 6-3). The risk falls within the acceptable range of 1 $H10^{-4}$ to 1 $H10^{-6}$ according to EPA policy (EPA 1990).

Adult Residents

Chronic hazard indices for health effects other than cancer were estimated for adult residents exposed to COPCs in surface soil via incidental ingestion and dermal contact with surface soil using specific exposure parameters. The total noncancer risk for adults was less than 1 under RME conditions, a HI of 0.3 (Table 6-1). Therefore, it is reasonable to assume that there will be no unacceptable noncancer risks to adult residents at the Former Pesticide Shop under the specified conditions of exposure.

Excess lifetime cancer risks associated with chronic exposure to surface soil were 3.0 $H10^{-5}$ under
RME conditions (Table 6-3). These risks fall within the acceptable range of 1 $H10^{-4}$ to 1 $H10^{-6}$ according to EPA policy (EPA 1990). There are no excess cancer health concerns for adult residents at the Former Pesticide Shop. However, the combined cancer risks for residential adults and children assuming an exposure duration of 30 years is 1 $H10^{-4}$.

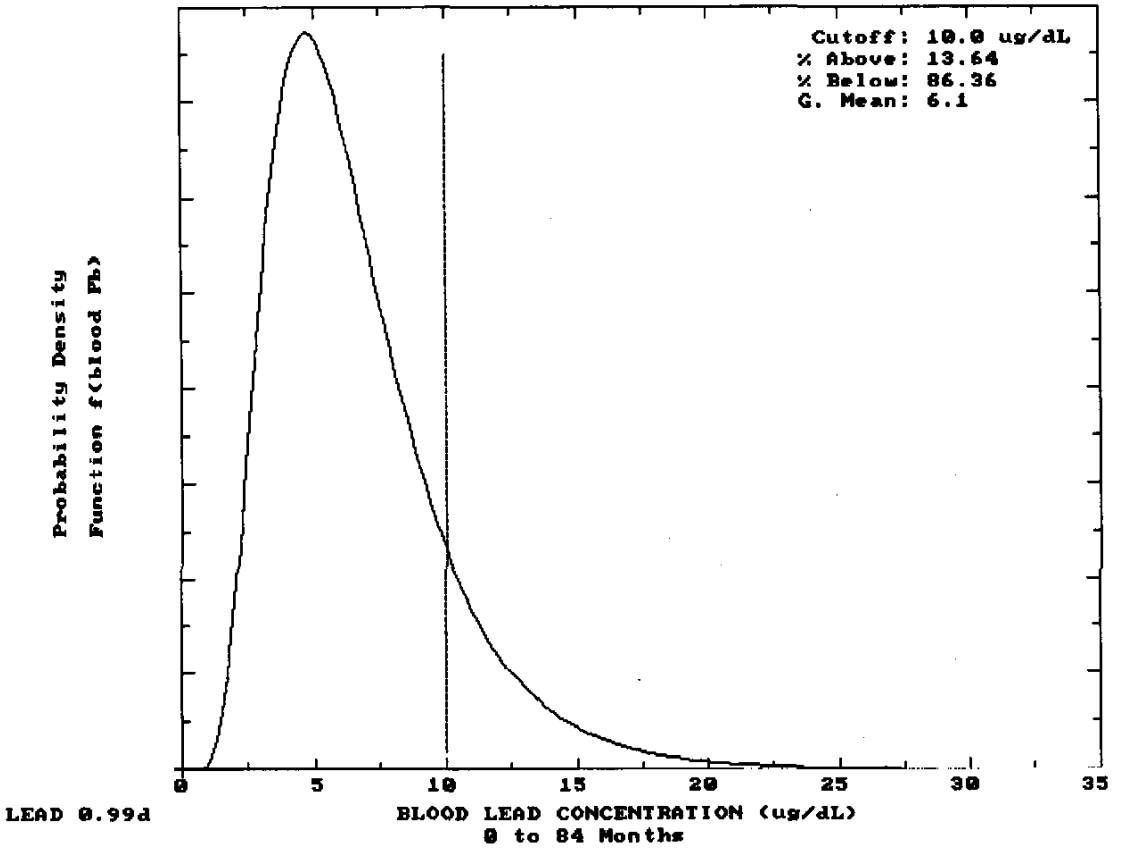


FIGURE 6-1. Graph of probability density of blood lead levels in children as modeled by the IEUBK model, at AOC 2

TABLE 6-1 SUMMARY OF CHRONIC RISKS, FOR HEALTH EFFECTS OTHER THAN CANCER FOR FUTURE RESIDENTIAL ADULTS AND CHILDREN AT AOC 2 AND AOC 3

Route of Exposure	AOC 2		AOC 3	
	Adult	Child	Adult	Child
Ingestion of Surface Soil	0.8	7.6	0.3	2.9
Dermal Contact with Surface Soil	0.07	1.2	0.04	0.8
Totals (HI)	0.9	8.8	0.3	3.7

TABLE 6-2 CHRONIC RISKS, FOR HEALTH EFFECTS OTHER THAN CANCER FOR FUTURE RESIDENTIAL CHILDREN AT AOC 2

COPCs	Child	
	Ingestion	**Dermal**
Aluminum	0.2	0.02
Antimony	1.7	0.3
Arsenic	1.3	0.07
Barium	0.05	0.0009
Cadmium	0.2	0.1
Chromium	0.2	0.4
Iron	2.5	0.05
Manganese	0.8	0.01
Mercury	0.3	0.005
Vanadium	0.2	0.2
Zinc	0.1	0.01
Benzo(a)anthrancene	- -	- -
Benzo(a)pyrene	- -	- -
Benzo(b)fluoranthene	- -	- -
Dibenz(a,h)anthracene	- -	- -
Indeno(1,2,3c-d)pyrene	- -	- -
Total (HI)	**7.6**	**1.2**

A- -≅ Toxicity values were not available to calculate risk.

TABLE 6-3 SUMMARY OF CANCER RISKS FOR FUTURE RESIDENTIAL ADULT AND CHILDREN AT AOC 2 AND AOC 3

Route of Exposure	AOC 2		AOC 3	
	Adult	**Child**	**Adult**	**Child**
Ingestion of Surface Soil	4 H 10 $^{-5}$	1 H 10 $^{-4}$	3 H 10 $^{-5}$	6 H 10 $^{-5}$
Dermal Contact with Surface Soil	6 H 10 $^{-7}$	3 H 10 $^{-6}$	3 H 10 $^{-6}$	1 H 10 $^{-5}$
Totals	4 H 10 $^{-5}$	1 H 10 $^{-4}$	3 H 10 $^{-5}$	7 H 10 $^{-5}$
Combined Adult and Child Risks (Exposure Duration = 30 yrs.)	1 H 10 $^{-4}$		1 H 10 $^{-4}$	

A- -≅ Toxicity values were not available to calculate risk.

TABLE 6-4 CANCER RISKS FOR FUTURE RESIDENTIAL CHILDREN AT AOC 2

COPCs	Child	
	Ingestion	Dermal
Aluminum	- -	- -
Antimony	- -	- -
Arsenic	5 H 10 $^{-5}$	3 H 10 $^{-6}$
Barium	- -	- -
Cadmium	- -	- -
Chromium	- -	- -
Iron	- -	- -
Manganese	- -	- -
Mercury	- -	- -
Vanadium	- -	- -
Zinc	- -	- -
Benzo(a)anthrancene	4 H 10 $^{-6}$	- -
Benzo(a)pyrene	3 H 10 $^{-5}$	- -
Benzo(b)fluoranthene	5 H 10 $^{-6}$	- -
Dibenz(a,h)anthracene	4 H 10 $^{-6}$	- -
Indeno(1,2,3c-d)pyrene	1 H 10 $^{-6}$	- -
Total	1 H 10 $^{-4}$	3 H 10 $^{-6}$

A- -≅ Toxicity values were not available to calculate risk.

TABLE 6-5 CHRONIC RISKS, FOR HEALTH EFFECTS OTHER THAN CANCER FOR FUTURE RESIDENTIAL CHILDREN AT AOC 3

COPCs	Child	
	Ingestion	**Dermal**
DDD	- -	- -
DDE	- -	- -
DDT	1.5	0.3
Alpha-Chlordane	0.3	0.08
Gamma-Chlordane	0.5	0.1
Heptachlor Epoxide	0.6	0.3
Total (HI)	**2.9**	**0.8**

A- -≅ Toxicity values were not available to calculate risk.

7. UNCERTAINTIES ASSOCIATED WITH RISK CHARACTERIZATION

This toxicological evaluation was based on conservative assumptions (i.e., likely overestimations of certain exposure parameters) where site-specific data were not available. There are considerable uncertainties associated with the exposure parameters and toxicological data used in the assessment of risks. Therefore, risk estimates may be either underestimated or overestimated but are more likely to be overestimated because of conservatism in both exposure and toxicity assumptions.

Risks for the pesticide chlordane have been quantified in this risk assessment with cis and trans chlordane and heptachlor epoxide. The chlordane mixture termed technical chlordane contains these chemicals, as well as other forms of chlordane such as cis and trans nonachlor. However, the quantified chlordane components cis chlordane, trans chlordane and heptachlor epoxide constitutes the largest proportion of technical chlordane. Thus, chlordane risks may be under estimated, but not significantly.

7.1 LEAD MODELING UNCERTAINTY

The lead model used in this evaluation has a number of limitations, some of which may overestimate risk (e.g., assumption of linearity at high-dose exposures when the kinetics of lead in the body indicate that the dose-response is nonlinear at high doses), and others which may underestimate risk (e.g., absorption rates and accumulation of lead in various body components vary among individuals and populations).

8. SUMMARY

The objective of this risk assessment was to evaluate the potential for adverse health effects to populations exposed to constituents of concern at AOC 2 and 3. Exposed populations include future adult and children residents. Potential adverse health effects were attributable to potential exposures to COPCs in surface soil. Exposures of the populations at the sites to the potential constituents of concern were characterized, and risks were estimated using the exposure information and toxicological data described in this document.

Oral and dermal exposures were considered for the relevant media with COPCs present. Attendant cancer and noncancer risks were estimated for the COPCs based on conservative assumptions using RME scenarios that are designed to avoid underestimating potential risks.

AOC 2 - Risks for health effects other than cancer (hazard quotients or hazard index) were less than one for residential adults. For residential children the hazard index was 8.8, driven by primarily to the exposure to arsenic and iron.

Total excess cancer risk for resident adults was 4 $H10^{-5}$, which fell in the acceptable range of 1 $H10^{-4}$ to 1 $H10^{-6}$. Total cancer risks for resident children was 1 $H10^{-4}$, which is the higher end of the acceptable range. Cancer risk for resident children was not driven by any one COPC. The following COPCs drove cancer risk: arsenic, benzo(a)anthracene, benzo(a)pyrene, benzo(b)fluoranthene, and indeno(1,2,3,c-d)pyrene. The combined cancer risk for both populations, assuming an exposure duration of 30 years, is 1 $H10^{-4}$.

Using the IEUBK model, a mean blood lead level of 6.1 µg/dL were predicted for exposed all children. Approximately 13.64% of all future residential children were predicted to have blood lead levels above 10 µg/dL. The predicted blood lead levels fall beneath the 10 µg/dL recommended cutoff, but more than 5% of the resident children will have blood lead levels above 10 µg/dL.

AOC 3 - Risks for health effects other than cancer (hazard quotients or hazard index) were less than one for residential adults. The HI was greater than 1 for residential children (HI = 3.7) driven mainly by future exposure to heptachlor epoxide and DDT with respective HQs of 0.9 and 1.8. The target organ for heptachlor epoxide and DDT toxicity is the liver.

Total cancer risks for resident adults and children ranged from 3 $H10^{-5}$ to 7 $H10^{-5}$, respectively, within the acceptable range of 1 $H10^{-4}$ to 1 $H10^{-6}$. The combined cancer risk for both populations, assuming an exposure duration of 30 years, fall on the higher end of the acceptable range of
1 $H10^{-4}$.

9. PRELIMINARY REMEDIATION GOALS (PRGs)

The goal of PRGs development is to derive COPC concentrations that will result in acceptable risks. These PRGs are used to aid in site management decisions and the development of remediation plans. To calculate the PRGs, target risk levels need to be identified. For noncancer effects, a concentration for each chemical is calculated that corresponds to a hazard index (HI) of 1.0 for all COPCs that affect a particular target organ. Carcinogenic PRGs are placed within the context of an acceptable cancer risk range, typically 1H 10^{-6} to 1 H 10^{-4}. While consistent with USEPA 1991 PRG guidance, each EPA Region has certain expectations for the presentation of PRG carcinogenic risk ranges. Region III was contacted, and they requested that a range of cancer risks be presented, including X H 10^{-6}, X H 10^{-5}, and 1H 10^{-4} where X represents the number of carcinogenic COPC at the site, and 1H 10^{-4} represents the upper limit of acceptable cancer risk.

The equation applied for the calculation of PRGs (USEPA 1991) taking into account site-specific exposure information was:

$$PRG_{copc} = Exposure\ Point\ Concentration\ H\ [Target\ Risk\ )\ Calculated\ Risk_{copc}],$$

For the exposure point concentration, the 95%UCLM is used.

In the case of lead, the goal of the PRG is to not exceed a blood lead level of 10 :g/dL and that no more than 5% of the children would have blood lead levels above 10 :g/dL. In order to determine the appropriate PRG concentration for lead, various mean soil concentrations were modeled in the IEUBK model to find a concentration that would fit the above criteria. Figures 9-1 to 9-3 show concentrations of each driver chemical at AOC 2 and AOC 3.

AOC 2

For AOC 2, noncancer human health risks were generally low for residential adults, but exceeded unity for residential children. Non-cancer risks that exceeded a HI of 1 for specific COPCs were evaluated for media-specific cleanup levels. All pathways and routes for the target risk group (residential children) was included in the calculation of PRGs for the surface soil media due to the presence of associated COPCs (antimony, arsenic, and iron).

Prior to derivation of PRGs for AOC 2 metals, the risk drivers (antimony, arsenic, iron, and lead were tested statistically to see if the site metal concentrations exceeded background concentrations. Background concentrations used for this statistical test are shown in Appendix D. If site metal concentrations were found to be no different from background concentrations, the PRG was not calculated.

First, the EPCs for the noncancer risk drivers were tested for normality using the Shapiro–Wilk test, $\forall = 0.05$ (Shapiro and Wilk 1965). Only validated samples were used in the calculation of the a representative concentration. "U" –qualified, or non-detect, samples were included in the calculations as one-half the detection limit. For duplicate samples, the higher concentration only was used in the calculations. If the data were not normally distributed they were transformed using the natural logarithm and tested for fit to a log-normal distribution (Table 9-1). After determining the distribution type, the analyte distributions were tested to see if site concentrations were significantly different from background concentrations using a Student t test ($\forall = 0.05$). Based on the appropriate Student t test, antimony and lead site concentrations were found to significantly exceed background concentrations. A PRG was therefore calculated for antimony at 27 mg/kg (Table 9-3). Although arsenic and iron at AOC 2 were not significantly different than background, highest concentrations of these elements, located at 2-SS-6 and 2-SS-7, may represent local hot the spots. However, these same stations contain high concentrations of other risk drivers, thus iron and arsenic will likely be addressed at the same the other risks are addressed.

Table 9-4 shows PRGs for the COPC (benzo(a)anthracene, benzo(a)pyrene, benzo(b)fluoranthene , dibenz(a,h)anthracene and indeno(1,2,3)pyrene) that drive the combined adult and child cancer risks at AOC 2. PRGs were calculated for various total target risks (5.0 H 10^{-6}, 5.0 H 10^{-5}, and 1.0 H 10^{-4}). Note that for total target risks of 5.0 H 10^{-5} and 1.0 H 10^{-4} the computed PRGs for the 4 COPC other than benzo(a)pyrene are higher than the actual Exposure Point Concentrations found at AOC 2.

Because PRGs exceeded the Exposure Point Concentration for four of the COPC an alternate PRG for benzo(a)pyrene has been computed. Target risks for the 4 COPC with actual Exposure Point Concentrations lower than the PRGs based on equal target risk have been held to existing values based on the present, maximum concentration as computed using the 95% UCML. The remainder of the target risk is then allocated to benzo(a)pyrene. When computed in this manner,

the PRGs for benzo(a)pyrene become 2.7 mg/kg at a total target risk of 5.0 H 10^{-5}, and 7.1 mg/kg at a total target risk of 1.0 H 10^{-4}.

Based on these assessments antimony and benzo(a)pyrene represent the greatest amount of risk at AOC 2.

A PRG was calculated for lead of 350 mg/kg in order to reach the goal of having the predicted blood-lead level exceed 10 :g/dL for no more than 5% of the population (See Figure 9-4). The PRG was calculated using the IEUBK model, and is essentially the same as the 400 mg/kg EPA screening value for lead in residential soil.

AOC 3

Noncancer human health risks at AOC 3 were generally low for residential adults, but exceeded unity for residential children. Noncancer risks that exceeded a HI of 1 for specific COPCs were evaluated for media-specific cleanup levels. Based on site-specific exposure data for AOC 3, the PRGs of specific COPCs were calculated to yield a target HI of 1 for one target organ (liver).

Table 9-5 presents the PRGs for the COPCs at AOC 3 for noncarcinogenic effects (for residential children) where the combined target risk (HI) is equal to 1 due to the same target organ toxicity (liver) of the COPCs. The COPCs identified as risk drivers are DDT, alpha-chlordane, gamma-chlordane, and heptachlor epoxide. The requirement to attain a total Hazard Index of less than or equal to 1 may be satisfied in different ways according to the allocation of risk among the different pesticides which contribute to the total risk. For example, when there are four contaminants, the level of each contaminant might be reduced to contribute 25 % of the risk, or contaminants A, B, and C might each be reduced to provide 10 % of the risk, which contaminant D would provide 70 % of the total risk.

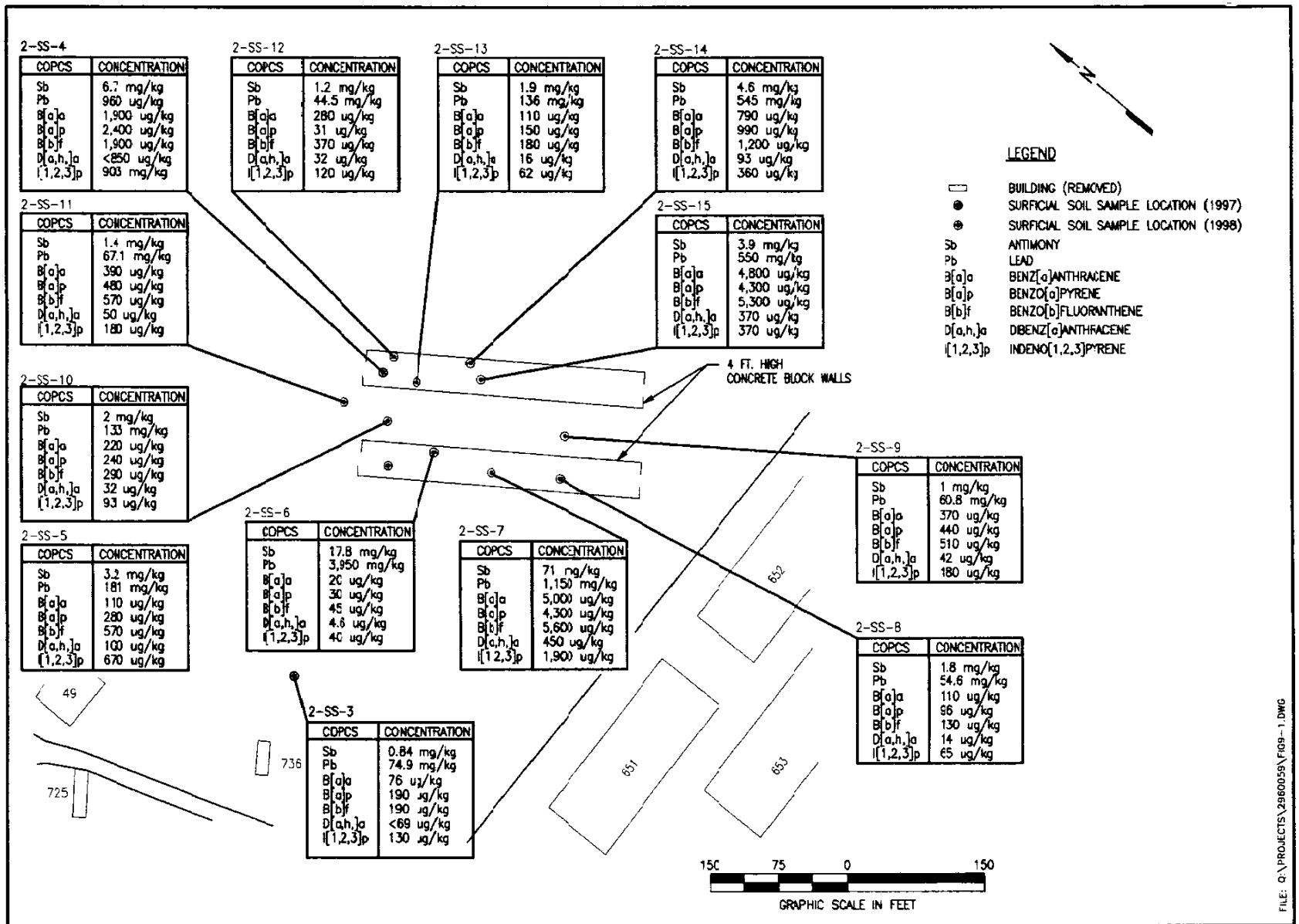
In the following table of noncarcinogenic risks from pesticides at AOC 3, the latter approach is used, with heptachlor epoxide contributing 60 % of the target hazard index, and the remaining three pesticides each contribute 13 %, for a total HI = 0.99. There are several reasons for taking this approach.

- This distribution requires that DDT, alpha- and gamma-chlordane be reduced below levels that would be acceptable with four equal 25% risk allocations. This allows the DDT, alpha-

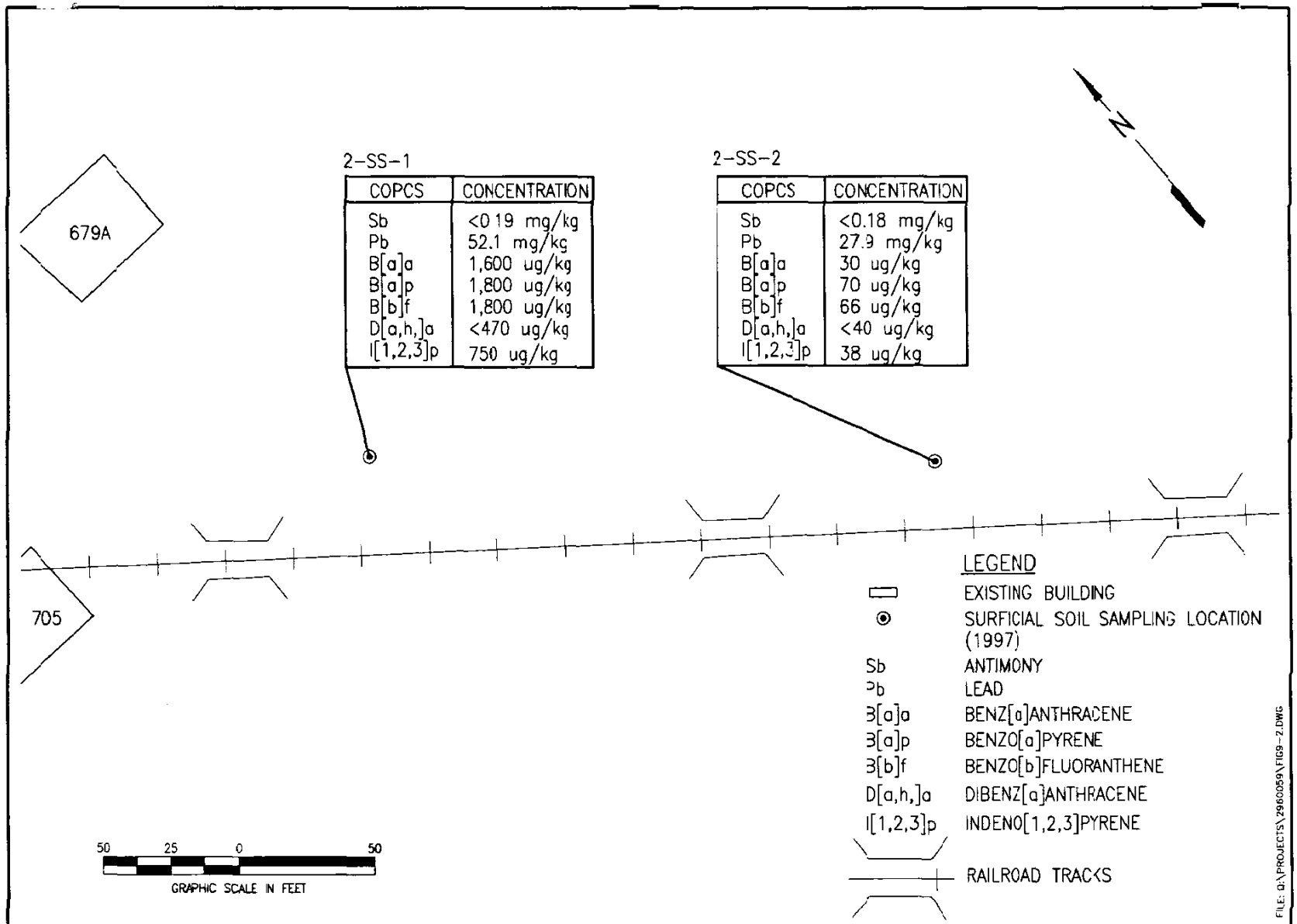
and gamma-chlordane levels to more closely approach favorable ecological risk levels. Since heptachlor epoxide contributes only fractionally to the eco-risk at pre-remediation levels, this cleanup approach would optimize both the non-cancer human health and ecological risk benefits.

- The exposure point concentrations for DDT, alpha- and gamma-chlordane are high relative to the heptachlor epoxide concentration (roughly 13 to 60 mg/kg, vs 0.65 mg/kg for heptachlor epoxide). From an operational standpoint, it will be easier to reduce to contaminant concentrations for the high level contaminants; likewise, the monitoring to evaluate successful reductions in the field will also be more easily accomplished for the high level concentrations.

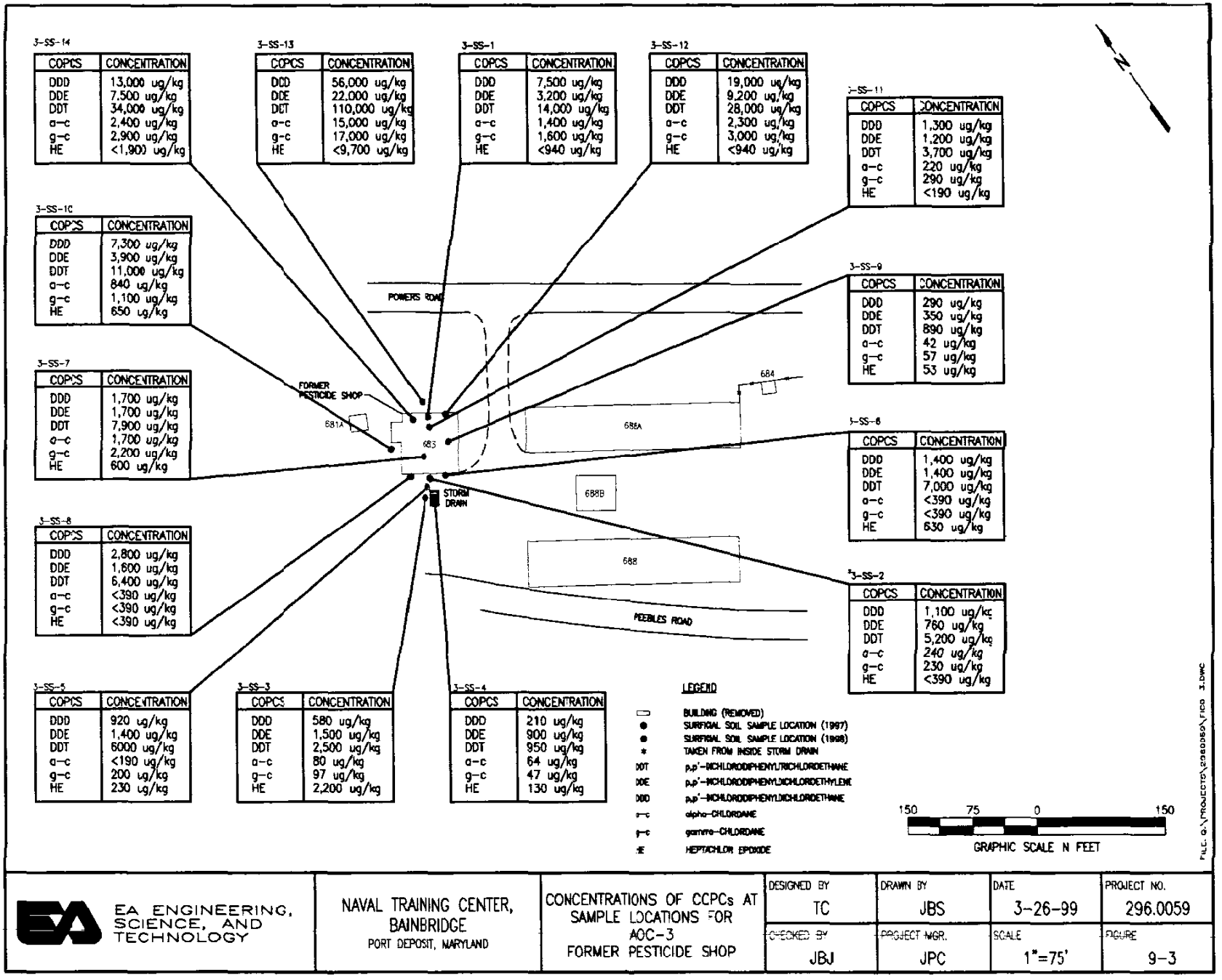
Table 9-6, shows PRGs for the COPCs (DDD, DDE, DDT, alpha-chlordane, gamma-chlordane and heptachlor epoxide) that drive cancer risks at AOC 3. PRGs are calculated for various total target risks (6.0E-06, 6.0E-05, and 1.0E-04).



EA ENGINEERING, SCIENCE, AND TECHNOLOGY	NAVAL TRAINING CENTER, BAINBRIDGE PORT DEPOSIT, MARYLAND	CONCENTRATION OF COPCs AT SAMPLE LOCATIONS 2-SS-3 THROUGH 2-SS-15 FOR AOC-2a FORMER OPEN STORAGE AREA/SALVAGE YARD	DESIGNED BY: TC	DRAWN BY: JBS	DATE: 3-26-99
			CHECKED BY: JBJ	PROJECT MGR.: JPC	SCALE: 1"=100'
					PROJECT NO.: 296.0059
					FIGURE: 9-1



EA ENGINEERING, SCIENCE, AND TECHNOLOGY	NAVAL TRAINING CENTER, BAINBRIDGE PORT DEPOSIT, MARYLAND	CONCENTRATIONS OF COPCs AT SAMPLE LOCATIONS 2-SS-1 AND 2-SS-2 FOR AOC-2b FORMER COAL STORAGE AREA	DESIGNED BY TC	DRAWN BY PMH	DATE 3-26-99	PROJECT NO. 296.0059
			CHECKED BY JBJ	PROJECT MGR. JPC	SCALE 1"=50'	FIGURE 9-2



EA ENGINEERING, SCIENCE, AND TECHNOLOGY	NAVAL TRAINING CENTER, BAINBRIDGE PORT DEPOSIT, MARYLAND	CONCENTRATIONS OF COPCs AT SAMPLE LOCATIONS FOR AOC-3 FORMER PESTICIDE SHOP	DESIGNED BY TC	DRAWN BY JBS	DATE 3-26-99	PROJECT NO. 296.0059
			CHECKED BY JBJ	PROJECT MGR. JPC	SCALE 1"=75'	FIGURE 9-3

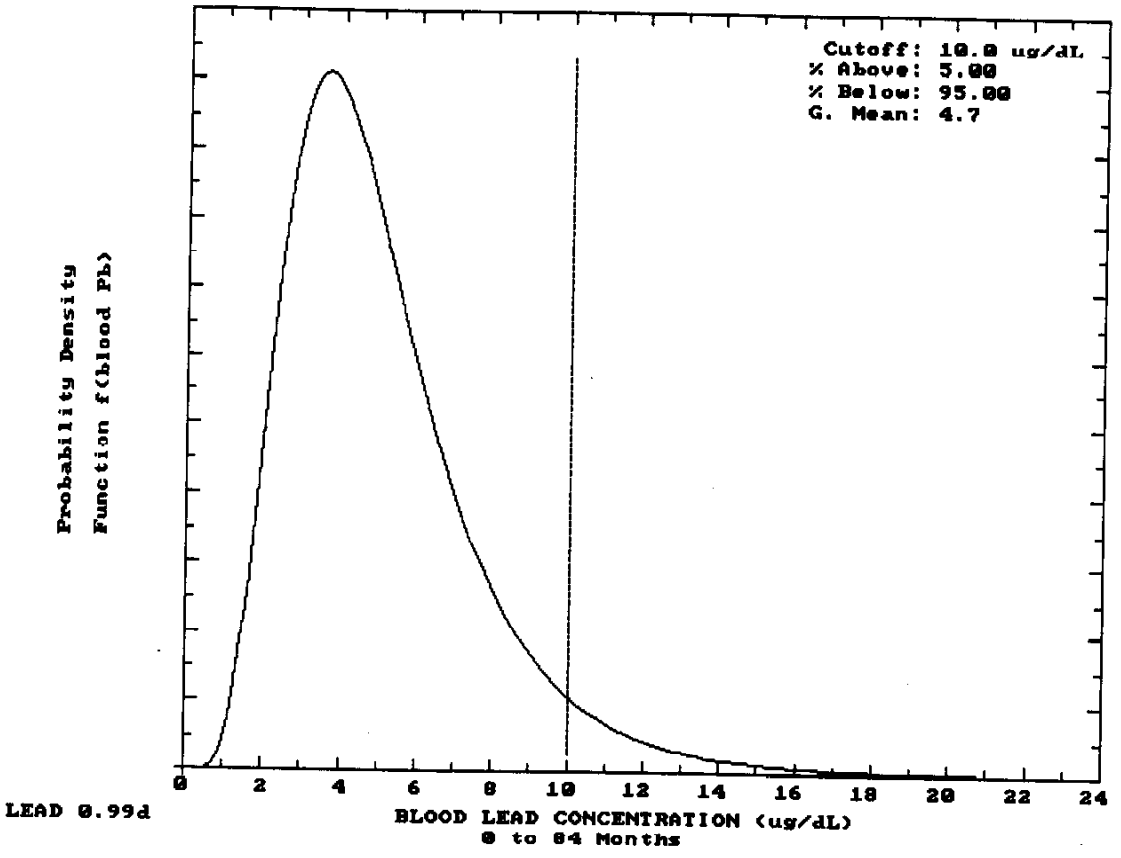


Figure 9-4. Graph of probability density of the blood lead levels in children as modeled by the IEUBK model, at AOC 2 for lead PRGs

TABLE 9-1 TEST FOR NORMALITY USING SHAPIRO WILKS FOR COPCS AT AOC 2

		Normal Distribution		Log Normal Distribution		
Analyte	n	Shapiro -Wilk statistic (W)	p (1)	Shapiro -Wilk statistic (W)	p (1)	Distribution
Antimony	15	0.443	0.0001	0.941	0.38	Lognormal
Arsenic	15	0.646	0.0001	0.942	0.4	Lognormal
Iron	15	0.585	0.0001	0.848	0.16	Lognormal
Lead	15	0.536	0.0001	0.911	0.14	Lognormal

TABLE 9-2 RESULTS OF STUDENT T TEST FOR COPCS AT AOC 2

Analyte	Variance Equal?	Probability> T	Site concentration > Background concentration
Antimony	No	0.0001	Yes
Arsenic	Yes	0.1612	no
Iron	Yes	0.2428	no
Lead	No	0.0039	Yes

TABLE 9-3 PRGs OF NONCARCINOGENIC EFFECTS FOR THE TARGET ORGAN -BLOOD AT AOC 2

COPC	Exposure Point Concentration (mg/kg)	HQ	Target Risk	PRG (mg/kg)
Antimony	54.3	2	1	27.15

Target HI = 1.0

TABLE 9-4 - PRGs OF CARCINOGENIC EFFECTS AT AOC 2

Total risk equal to target risk: 5 H 10^{-6}

COPC	Exposure Point Concentration (mg/kg)	Risk	Target Risk	PRG (mg/kg)
Benzo(a)anthracene	5	5.7 H 10^{-6}	1.0 H 10^{-6}	0.9
Benzo(a)pyrene	4.3	4.9 H 10^{-5}	1.0 H 10^{-6}	0.09
Benzo(b)Fluoranthene	5.6	6.4 H 10^{-6}	1.0 H 10^{-6}	0.9
Dibenz(a,h)anthracene	0.45	5.1 H 10^{-6}	1.0 H 10^{-6}	0.09
Indeno(1,2,3,c-d)pyrene	1.8	2.1 H 10^{-6}	1.0 H 10^{-6}	0.9

Total risk equal to target risk: 5 H 10^{-5}

COC	Exposure Point Concentration (mg/kg)	Risk	Target Risk	PRG (mg/kg)
Benzo(a)anthracene	5	5.7 H 10^{-6}	1.0 H 10^{-5}	8.8
Benzo(a)pyrene	4.3	4.9 H 10^{-5}	1.0 H 10^{-5}	0.9
Benzo(b)fluoranthene	5.6	6.4 H 10^{-6}	1.0 H 10^{-5}	8.8
Dibenz(ah)anthracene	0.45	5.1 H 10^{-6}	1.0 H 10^{-5}	0.9
Indeno(123)pyrene	1.8	2.1 H 10^{-6}	1.0 H 10^{-5}	8.8

Total risk equal to target risk: 5 H 10^{-4}

COC	Exposure Point Concentration (mg/kg)	Risk	Target Risk	PRG (mg/kg)
Benzo(a)anthracene	5	5.7 H 10^{-6}	2.0 H 10^{-5}	17.5
Benzo(a)pyrene	4.3	4.9 H 10^{-5}	2.0 H 10^{-5}	1.8
Benzo(b)fluoranthene	5.6	6.4 H 10^{-6}	2.0 H 10^{-5}	17.5
Dibenz(ah)anthracene	0.45	5.1 H 10^{-6}	2.0 H 10^{-5}	1.8
Indeno(123)pyrene	1.8	2.1 H 10^{-6}	2.0 H 10^{-5}	17.5

Total Risk = 5.0 H $^{-05}$, Target risk normalized to exposure point concentration

COC	Exposure Point Concentration (mg/kg)	Risk	Target Risk	PRG (mg/kg)
Benzo(a)anthracene	5	5.7 H 10 $^{-6}$	5.7 H 10 $^{-6}$	5.0
Benzo(a)pyrene	4.3	4.9 H 10 $^{-5}$	3.1 H 10 $^{-5}$	2.7
Benzo(b)fluoranthene	5.6	6.4 H 10 $^{-6}$	6.4 H 10 $^{-6}$	5.6
Dibenz(ah)anthracene	0.45	5.1 H 10 $^{-6}$	5.1 H 10 $^{-6}$	0.5
Indeno(123)pyrene	1.8	2.1 H 10 $^{-6}$	2.1 H 10 $^{-6}$	1.8

Total Risk =1.0 H $^{-04}$, Target risk normalized to exposure point concentration

COC	Exposure Point Concentration (mg/kg)	Risk	Target Risk	PRG (mg/kg)
Benzo(a)anthracene	5	5.7 H 10 $^{-6}$	5.7 H 10 $^{-6}$	5.0
Benzo(a)pyrene	4.3	4.9 H 10 $^{-5}$	8.1 H 10 $^{-5}$	7.1
Benzo(b)fluoranthene	5.6	6.4 H 10 $^{-6}$	6.4 H 10 $^{-6}$	5.6
Dibenz(ah)anthracene	0.45	5.1 H 10 $^{-6}$	5.1 H 10 $^{-6}$	0.5
Indeno(123)pyrene	1.8	2.1 H 10 $^{-6}$	2.1 H 10 $^{-6}$	1.8

TABLE 9-5 PRGs OF NONCARCINOGENIC EFFECTS FOR THE TARGET ORGAN- LIVER AT AOC 3

COPC	Exposure Point Concentration (mg/kg)	HQ	Target Risk	PRG (mg/kg)
DDT	59.3	1.7	0.13	4.3
Alpha Chlordane	13.2	0.4	0.13	4.1
Gamma Chlordane	17	0.5	0.13	4.1
Heptachlor Epoxide	0.65	1.0	0.6	0.4
		Target HI =	1	

TABLE 9-6 PRGs OF CARCINOGENIC EFFECTS AT AOC 3

COPC	Exposure Point Concentration (mg/kg)	Risk	Target Risk	PRG (mg/kg)
DDD	53	2.3×10^{-5}	1.0×10^{-6}	2.3
DDE	9.6	5.9×10^{-6}	1.0×10^{-6}	1.6
DDT	59.3	3.6×10^{-5}	1.0×10^{-6}	1.6
Alpha Chlordane	13.2	8.5×10^{-6}	1.0×10^{-6}	1.5
Gamma Chlordane	17	1.1×10^{-5}	1.0×10^{-6}	1.5
Heptachlor Epoxide	0.65	1.4×10^{-5}	1.0×10^{-6}	0.05
Total Target Risk =			6.0×10^{-6}	

COPC	Exposure Point Concentration (mg/kg)	Risk	Target Risk	PRG (mg/kg)
DDD	53	2.3×10^{-5}	1.0×10^{-5}	23.1
DDE	9.6	5.9×10^{-6}	1.0×10^{-5}	16.3
DDT	59.3	3.6×10^{-5}	1.0×10^{-5}	16.3
Alpha Chlordane	13.2	8.5×10^{-6}	1.0×10^{-5}	15.5
Gamma Chlordane	17	1.1×10^{-5}	1.0×10^{-5}	15.5
Heptachlor Epoxide	0.65	1.4×10^{-5}	1.0×10^{-5}	0.5
Total Target Risk =			6.0×10^{-5}	

COPC	Exposure Point Concentration (mg/kg)	Risk	Target Risk	PRG (mg/kg)
DDD	53	2.3×10^{-5}	1.66×10^{-5}	38.3
DDE	9.6	5.9×10^{-5}	1.66×10^{-5}	27.0
DDT	59.3	3.6×10^{-5}	1.66×10^{-5}	27.0
Alpha Chlordane	13.2	8.5×10^{-5}	1.66×10^{-5}	25.8
Gamma Chlordane	17	1.1×10^{-5}	1.66×10^{-5}	25.8
Heptachlor Epoxide	0.65	1.4×10^{-5}	1.66×10^{-5}	0.8
Total Target Risk =			1.0×10^{-4}	

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APPENDIX A: EXPOSURE PARAMETERS

Table A-1. Summary of Exposure Parameter Values in Estimating All Exposure Scenarios

$$\textit{Soil Ingestion CDI} = \frac{C_{Soil} * IR * EF * ED * 1E\text{-}6\ kg/mg}{BW * AT}$$

$$\textit{Dermal Contact with Soil CDI} = \frac{C_{Soil} * SA * ABS * AF * EF * ED * 1E\text{-}6\ kg}{BW * AT}$$

Parameter	Value to Estimate: RME	Rationale	Reference
Global variables			
Body Weight (kg)			
- Adults	70	Average of males and females between 18 and 65 years.	EPA 1993
- Children	15	Average of males and females 6 years old.	EPA 1997
Exposure Duration (yr)			
- Adults	24	Time one resides in one home.	BPJ/EPA 1993
- Children	6	Time a child may be significantly exposed to environmental media.	
Averaging Time (days)			
- Cancer risks	25,550	Based on 70-year life expectancy.	EPA 1989
- Noncancer risks			
- Adults	8,760	Based on exposure duration.	
- Children	2,190	Based on exposure duration.	
Relative Absorption Factors			
- Dermal contact with soil			
VOC	0.25	For chemicals with high sorption to soils.	EPA 1995
PAH	0.10	For chemicals with low sorption to soils.	
PCB	0.06	For chemicals with low sorption to soils.	
Pesticides	0.10	For chemicals with low and high sorption to soils, respectively.	
Inorganic Analytes	0.01	Recommended value	

Parameter	Value to Estimate: RME	Rationale	Reference
Arsenic - Ingestion of soil	0.032 1	Recommended value For all chemicals.	 EPA 1995
Exposure Frequency (day/yr)	350	Assumes 15 days of vacation per year.	
Fraction of Exposed Skin that Contacts Soil	1	Numerical value indicating percentage of exposed skin that contacts the medium	BPJ
Future Adult Resident			
Ingestion Rate of Soil (mg/day)	100	Ingestion rate for adults	EPA 1993
Dermal Contact with Soil Available skin surface area (cm^2)	3,000	Assumes exposed skin surface area for hands, face, and arms.	BPJ/EPA 1997
Adherence Factor for Soil (mg/cm^2)	0.03	The amount of a specified matrix that can be contained on the skin	BPJ/EPA 1992
Future Child Resident			
Incidental Ingestion of Soil - Ingestion rate (mg/day)	200	Average ingestion rate for children ages 1 through 6.	EPA 1993
Dermal Contact with Soil - Available skin surface area (cm^2)	1,800	Assumes exposed skin surface area for hands, face, and arms.	BPJ/EPA 1997
Adherence Factor for Soil (mg/cm^2)	0.2	The amount of specified matrix likely to be contained on skin of children	BPJ/EPA 1992

BPJ Best Professional Judgement

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APPENDIX B: TOXICITY PROFILES

TOXICITY PROFILES FOR COPC

Aluminum

Health effects research in humans and animals has shown that elevated levels of aluminum in the body may be toxic, particularly to the central nervous, skeletal and hematological systems. Much of aluminum toxicity depends on variations in absorption and chemical form of the aluminum complexes and oxidation states and interactions with dietary constituents. The toxicity of aluminum can be divided into three major categories: (1) the effect of aluminum compounds in the gastrointestinal tract following ingestion, (2) the effect in the lungs following inhalation, and (3) systemic toxicity of aluminum (ATSDR 1990a). Aluminum compounds can alter absorption of other elements in the gastrointestinal tract (*i.e.*, fluoride, calcium, iron, cholesterol, phosphorus) and alter gastrointestinal tract mobility by inhibition of acetylcholine-induced contractions. Inhalation of aluminum dusts can lead to the development of pulmonary fibrosis, producing both restrictive and obstructive pulmonary disease. One of the greatest health concerns is aluminum=s proposed association with chronic encephalopathy in humans (Ganrot 1986). A progressive fatal neurologic syndrome has been noted in patients on long-term intermittent hemodialysis treatment for chronic renal failure and may be due to aluminum intoxication. Symptoms in these patients include a speech disorder followed by dementia, convulsions, and myoclonus. Aluminum content of brain, muscle, and bone tissues is increased in these patients. Sources of the excess aluminum may be from oral aluminum hydroxide commonly given to these patients or from aluminum in dialysis fluid derived from tap water used to prepare the dialysate fluid.

Minimal neurotoxicity in the offspring of mice exposed to aluminum lactate has been observed (Golub et al. 1995). Groups of 16 pregnant Swiss-Webster mice were fed 25 (control group), 500, or 1000 mg Al/kg of aluminum lactate throughout gestation and lactation (Donald et al. 1989). No treatment-related changes were observed in maternal survival, body weight, food intake, toxic signs or neurobehaviour. A battery of neurobehavioral tests performed on pups showed that a significant (p=0.007) number of pups in the high dose group had impaired vertical screen climb performance. In the low dose group, equivalent to 100 mg/kg-day, decreased forelimb grip strength and increased foot splay distance were observed.

The available systemic toxicity data on aluminum have been evaluated and found to be inadequate for quantitative risk assessment (U.S. EPA 1996). The value for the chronic oral RfD (1 mg/kg-day) was obtained from the U.S. EPA Environmental Criteria Assessment Office, Cincinnati, Ohio, based on a LOAEL of 100 mg/kg-day for neurotoxicity, with an uncertainty factor of 100.

The oral RfD value is 1.0 mg/kg-day. A dermal RfD of 0.2 mg/kg-day was estimated by multiplying the oral RfD by $2H10^{-1}$ (or, 20%) (U.S. EPA 1998).

The U.S. EPA (1998) has not established SFs for aluminum.

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Antimony

The carcinogenicity of antimony (Sb) has been classified as Category D (no human data and inadequate data from animal bioassays) by the U.S. EPA (1998).

Therapeutic administration of antimony-containing compounds has produced cardiac effects, liver toxicity, pulmonary congestion, skin reactions, vomiting, diarrhea, gastric discomfort, and ulcers in treated humans (ATSDR 1990c). Inhalation exposures in industrial settings have produced respiratory tract irritation, pneumoconiosis, and impaired pulmonary function in workers (Cooper *et al*. 1968; Potkonjak and Vishnijich 1983). Dermatosis and ocular irritation have also been reported in humans following exposure to airborne antimony (Potkonjak and Vishnijich 1983).

The U.S. EPA has established an oral RfD of $4H10^{-4}$ mg/kg-day for antimony, based on altered longevity, blood glucose, and cholesterol content, and including an aggregate uncertainty factor of 1,000 (U.S. EPA 1998). The uncertainty factor accounts for interspecies and intraspecies extrapolation (10-fold each) and subchronic to chronic NOAEL extrapolation (10-fold).

Because there are insufficient data to quantify the adverse effects of exposure to antimony via the inhalation route, the oral toxicity value is used for chronic exposure scenarios. There is no dermal RfD for antimony. Therefore, the oral RfD for antimony was adjusted with an oral absorption fraction of $2H10^{-1}$ (or, 10%) (ATSDR 1992). The dermal RfD is $4H10^{-5}$ mg/kg-day.

There are no cancer SFs for antimony.

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ARSENIC

Arsenic (As, MW 74.9, CAS registry number 7440-38-2) is an ubiquitous metalloid present in the environment from natural and anthropogenic sources. Arsenic is a natural component of the earths crust. It originates from natural sources such as volcanoes and erosion from mineral deposits, but also from human activities such as chemical production and use, coal combustion, and waste disposal. Arsenic can exist in several different valence states and in many different inorganic and organic forms. The form of arsenic with the greatest commercial importance is inorganic arsenic trioxide (As_2O_3), which is produced from flue dust collected during the smelting of copper and lead. There has been no commercial production of As_2O_3 in the United States since 1985, although it is imported for industrial use.

Arsenic is one of the most widely studied toxicants. Analysis of the toxic effects of arsenic is complicated by the fact that arsenic can exist in several different inorganic and organic compounds. Most cases of human toxicity have been associated with exposure to inorganic arsenic (ATSDR 1993). While As_2O_3 is the most common inorganic arsenical in air, a variety of inorganic trivalent arsenites or pentavalent arsenates occur in water, soil, and food (ATSDR 1993). Trivalent arsenites are somewhat more toxic than pentavalent arsenates (EPA 1995a); however, the difference in relative potency is small. An additional complexity in the analysis of arsenic toxicity is that there are no suitable animal models for carcinogenicity.

Cancer

EPA has classified arsenic as a human carcinogen (Category A), based on observations of increased lung cancer mortality in populations exposed mainly via inhalation and of increased skin cancer

incidence in populations consuming drinking water containing high concentrations of arsenic (EPA 1995a).

There is evidence from a large number of occupational epidemiologic studies that high-dose inhalation exposure to inorganic arsenic is associated with an increase in lung cancer. Most studies involve workers exposed primarily to arsenic trioxide dust in air at copper smelters (e.g., Enterline et al.1987; Enterline and Marsh 1982; Axelson et al.1978), but increased incidence of lung cancer has also been observed at chemical plants where exposure was primarily to arsenate (Ott et al.1974; Sobel et al.1988). Although several studies suggest that residents living near smelters or arsenical chemicals may also have increased risk of lung cancer (Pershagen 1985; Brown et al.1984), the increases are small and may not be biologically significant (e.g., Frost et al.1987).

Several human studies provide sufficient exposure data to permit quantification of cancer risk (Tseng et al.1968; Tseng 1977). In general, the data indicate that there is an approximately linear increase in relative risk as a function of increasing cumulative exposure (EPA 1995a). Animal studies do not show evidence of a carcinogenic effect from inhalation exposure of arsenic (EPA 1995a); however, two intratracheal instillation studies in hamsters have demonstrated that both arsenite and arsenate can increase the incidence of lung adenomas and/or carcinomas (Ishinishi et al.1983; Pershagen and Bjorklund 1985).

One of the most reliable epidemiologic studies that provides dose-response data is the investigation by Tseng et al. (1968). In this study, the quantitative risk of skin cancer from exposure to inorganic arsenic by ingestion was examined. In this investigation, 40,421 people in Taiwan were exposed to arsenic in drinking water at levels ranging from 100 to 1,800 µg/L. The control population consisted of 7,500 people who were exposed to nondetectable levels up to 17 µg/L arsenic in drinking water. Results showed an age- and dose-dependent increase in the incidence of skin cancer in the exposed population, while there were no arsenic-related skin cancers detected in the control population. EPA used this study to calculate a unit risk of 5×10^{-5} based on lifetime exposure to water containing 1 µg/L arsenic.

Mutagenicity

Arsenic has been tested in a range of prokaryotic and eukaryotic systems. In general, arsenic is either inactive or extremely weak as an inducer of gene mutations *in vitro*; however, it is clastogenic and induces sister chromatid exchanges in a variety of cell types, including human cells (ATSDR 1993). Arsenic does not appear to induce chromosome aberrations *in vivo* in experimental animals; however, it may do so in humans (NRC 1977). Several studies also suggest that arsenic may affect DNA by the inhibition of DNA repair processes or by base-pair substitution (ATSDR 1993).

Toxicity

Epidemiologic Data in Humans

Workers exposed to arsenic dusts in air may experience irritation to the mucus membrane of the nose and throat, which may lead to laryngitis, bronchitis, or rhinitis (Morton and Caron 1989). Very high exposures may cause perforation of the nasal septum (Pinto and McGill 1953). These effects, including perforation, were usually mild and did not result either in impaired respiration or illness. Several studies revealed that inhalation of high levels of arsenic dust or fumes led to nausea, vomiting, and diarrhea in workers (Beckett et al. 1986; Bolla-Wilson and Bleecker 1987; Morton and Caron 1989). Neurological injury may occur in humans after inhalation of inorganic arsenic, including peripheral neuropathy of sensory and motor neurons (numbness, loss of reflexes, muscle weakness) (Feldman et al. 1979; Landau et al. 1977). Hallucinations, agitations, emotional lability, and memory loss may also result (Beckett et al. 1986; Morton and Caron 1989). Adverse neurological effects tend to diminish, but may persist past exposure period (Beckett et al. 1986).

Developmental effects of arsenic exposure have been implicated in the unborn fetuses of pregnant women living near a copper-smelting plant in Bulgaria (Tabacova 1986). Fatal defects (e.g., small forebrains and underdeveloped earpits) occurred at a rate of 3.6 per 1,000 live births, which is three times the national rate. From a cohort of about 15,000 women living near the plant, increased placental concentration of arsenic, elevated lipid peroxides, and decreased GSH in maternal and cord blood were found. This suggested that arsenic was responsible for the oxidative damage in the pathogenesis of prenatal birth defects. The hypothesis was tested in an experimental *in vitro* mouse embryo model.

Experimental Studies in Animals

Systemic Toxicity

Chronic exposure of experimental animals to arsenic have been described by several studies. Tissues which are adversely affected by arsenic exposure include the gastrointestinal, cardiovascular, hematopoietic, renal, nervous, and respiratory systems.

In a chronic toxicity study, beagle dogs (6/group) were fed sodium arsenate or sodium arsenite at dosed of 5, 25, 50, or 125 ppm arsenic in the diet, which corresponds to an average daily dose of 0.2, 1.0, 2.1, or 5.2 mg As/kg-day assuming a body weight of 12 kg for each dog (Byron et al. 1967). Four out of six dogs fed the highest dose of As died within 9 months. The main effects were anorexia and listlessness, with weight loss of 44B61 percent from the beginning of the study. Moderate anemia and atrophy of numerous tissues were revealed after hematologic and histologic examinations. A chronic NOAEL of 2.1 mg As/kg-day was identified in dogs since there was no difference between controls and dogs fed 50 ppm As^{3+} or As^{5+} in their diet.

In a 1-year study involving rhesus monkeys were exposed to As^{5+} (in the form of $2Na_3(PO_4AsO_4VO_4)$AANaF@ $18H_2O$) in milk at doses of 2.8 mg/kg-day (3-day and 8-week old

monkeys) and 5.7 mg/kg-day (8-weeks old) (Heywood and Sortwell 1979). Effects seen in one monkey dosed with 2.8 mg As/kg-day beginning at 3 days of life included sudden weakness, dehydration along with bronchopneumonia, hemorrhage, edema, and necrosis in the brain. Another animal from the highest dose of arsenic, had acute inflammation of the small intestine and moderate regression of the thymus. Surviving animals had normal EEGs and normal levels of neurological function. There was no evidence of delayed toxicity in surviving animals.

Male weanling Sprague-Dawley rats (10/group) were exposed to 0 or 50 µg/mL sodium arsenate for 320 days in drinking water (Carmignani et al. 1983). Histological examination revealed that the liver and kidneys accumulated significant levels of arsenic at 25.2 and 43.0 mg/kg, respectively, and swollen hepatocytes were noted near the centrilobular veins of the liver. Focal changes in the glomerulus and tubules were seen in the kidneys. No changes were noted in the myocardium, gastrocnemius, arterial vessels, lungs, brain, or sciatic nerves. Sympathetic hyperactivity, hypersensitivity, or both were induced by arsenic, and the authors speculated that these findings may explain the cardiovascular effects in people chronically exposed to arsenic.

CD male and female mice were fed 5 mg As^{3+}/L sodium arsenite in their drinking water, which corresponds to 0.35 mg/kg-day, in a special environment designed to minimize exposure to trace metals (Schroeder and Balassa 1967). After 180 days, growth rate and body weights were not affected, but a decrease in body weight in males was apparent after 360 and 540 days. There was also a decrease in survival rates at 18 months in males and 21 months in females, with a median life span that was reduced by 74 and 76 days in males and females, respectively.

Developmental Toxicity

High levels of arsenic can cause developmental effects in animals. Slight decreases in fetal weight resulted after mice were exposed to 2 mg As/m^3 as As_2O_3 on days 9B12 of gestation. Higher levels of arsenic (20 mg/m^3) produced skeletal malformations and an increase in fetal deaths (Nagymajtenyi et al. 1985). Other studies have reported an increase in fetal mortality from 2B68 mg As/kg-day sodium arsenite (Baxley et al. 1981; Hood and Harrison 1982). Baxley et al. (1981) exposed pregnant CD-1 mice to single oral doses of 1, 20, 40, or 45 mg/kg sodium arsenate by gavage on days 8B15 of gestation. The frequency of dead or resorbed fetuses was significantly elevated in animals exposed to 40 or 45 mg/kg on days 10, 12, 13, 14, or 15 of gestation. Hood and Harrison (1982) exposed pregnant hamsters to a single gavage dose of 25 mg/kg sodium arsenite on days 8, 11, or 12 of gestation, or 20 mg/kg on days 9 or 10. Prenatal mortality was significantly elevated in animals dosed with 25 mg/kg on gestational days 8 or 12. Small increases in the percentage of fetuses that were malformed were noted in treated groups, although these were not significant. Similarly, Hood and Harrison (1982) performed a similar experiment in hamsters dosed by a single intraperitoneal amount of 5 mg/kg sodium arsenite on days 8, 11, or 12, or 2.5 mg/kg on days 9 or 10 of gestation. Again, prenatal mortality was elevated, and although there were small increases in malformations, they were not significant. Hood and Harrison concluded that arsenite is significantly less toxic when administered orally than intraperitoneally. Intraperitoneal injections of 45 mg/kg sodium arsenite on days 6B12 of gestation in pregnant Swiss-Webster mice resulted in the following fetal malformations: exencephaly, micrognathia, protruding tongue, agnathia, open eye,

exophthalmos, anophthalmia, missing pinna, cleft lip, hydrocephalus, umbilical hernia, eventration, ectrodactyly, micromelia, limb and tail malformations, and skeletal defects. Similar adverse effects were seen in exposed Wistar rat fetuses (Beaudoin 1974), golden hamsters (Willhite 1981; Carpenter 1987).

Fetal mortality was increased and malformation resulted in experimental animals exposed to organic forms of arsenic. Albino CD rats and CD-1 mice given repeated doses DMA, a metabolite of arsenic, during gestation had significantly elevated fetal mortality and showed developmental effects: skeletal anomalies (delayed ossification and supernumerary ribs), malformed palate, cleft lip, reduced fetal weight (Rogers et al. 1981).

Reproductive Toxicity

There was one study that examined the reproductive toxicity of arsenic in animals. In a three-generation study in Charles River mice given sodium arsenate in drinking water at an average dose of 0.35 mg As^{3+}/kg-day, there were no significant effects detected, although a trend toward a decreased number of pups per litter and slightly altered male:female sex ratios were observed (from 1.03 to 1.30 in the F_2 generation, and from 1.00 to 1.71 in the F_3 generation (Schroeder and Mitchener 1971).

In another study, male and female Harlan/ICR Swiss mice dosed 3 times per week for 10 weeks with 0, 11.9, or 119 mg/kg-day MMA, a metabolite of As, prior to mating and during gestation produced fewer litters than normal (Prukop and Savage 1986). None of the animals receiving the highest dose of MMA produced litters, and only 50 percent of the animals dosed with 11.9 mg/kg-day MMA produced litters, compared with 80B100 percent in controls. This was attributed to decreased fertility of the male mice.

Other Systemic Effects

No studies have been located that discuss other systemic effects of exposure to arsenic in experimental animals.

Toxicokinetics

Most of the existing data on the toxicokinetics of arsenic is on the inorganic form. Both arsenate and arsenite are well absorbed by both the oral and inhalation routes.

Arsenic in air exists as particulate matter and absorption by inhalation involves deposition of the particles onto the surface of the lungs and absorption of arsenic from the deposited material. Deposition was estimated to be about 40 percent and absorption was 75B85 percent in lung cancer patients exposed to arsenic in cigarette smoke (Holland et al. 1959), making the percentage of inhaled arsenic 30B34 percent. Animal studies on As (i.e., sodium arsenite, sodium arsenate, and arsenic trioxide) via intratracheal instillation suggested that nearly all of the deposited material was absorbed, because clearance of the compounds from the lungs was rapid and nearly complete (60B90

percent cleared within 1 day) (Marafante and Vahter 1987; Rhoads and Sanders 1985). In contrast, insoluble forms of As (i.e., arsenic sulfide and lead arsenate) cleared more slowly, suggesting that the rate of absorption is lower for the insoluble forms of arsenic (ATSDR 1993).

Absorption of arsenates and arsenites across the gastrointestinal tract is nearly complete. Measurements of human fecal excretions given oral doses of arsenite reported that less than 5 percent was recovered, indicating that absorption was about 95 percent (Bettley and O=Shea 1975). Again, ingestion of less insoluble forms of arsenic such as arsenic triselenide did not lead to a high percentage of absorption across the gastrointestinal tract (Mappes 1977).

The data on dermal absorption of inorganic arsenic are limited and not quantitative.

Once absorbed, arsenic is distributed throughout the body to the liver, kidney, skeleton, gastrointestinal tract, and other tissues. Autopsies of people exposed to background levels of arsenic revealed that arsenic is present in all tissues of the human body at approximately comparable concentrations (Liebscher and Smith 1968). Absorbed arsenic can also cross the placenta and be distributed to fetuses (Hood et al. 1987, 1988). The metabolites of both inorganic and organic arsenic appeared to be distributed equally in all body tissue following oral exposure (Takahashi et al. 1988; Yamauchi and Yamamura 1984, 1985; Stevens et al. 1977; Yamauchi et al. 1988).

Several *in vivo* and *in vitro* studies have elucidated the metabolic and detoxification pathway for arsenic in mammals (Vahter 1981; Vahter and Envall 1983; Hirata et al. 1988; Marafante and Vahter 1987; Takahashi et al. 1988; Maiorino and Aposhian 1985; Marafante et al. 1985; Vahter and Marafante 1983), including humans (Buchet et al. 1981a,b; Crecelius 1977; Lovell and Farmer 1985; Smith et al. 1977; Tam et al. 1979; Vahter 1986), and have been reviewed by Thompson (1993). Analysis of urinary excretion products from humans and animals revealed increased levels of inorganic As^{3+}, As^{5+}, methylarsonic acid (MMA), and dimethylarsonic acid (DMA). The metabolism of inorganic arsenic involve two processes: oxidation/reduction of As^{5+} and As^{3+} species and methylation. Specifically, inorganic arsenic is converted via methylation in the liver to MMA and to DMA, which is the principal metabolite. Both MMA and DMA form conjugates with glutathione or glutathione derivatives and are excreted in urine. Since methylation is enzyme-dependent, saturation kinetics appear to determine the toxicity, or carcinogenicity, of arsenic in humans. At low doses, arsenic can be effectively detoxified; whereas at higher doses, the detoxification pathway may become increasingly saturated, thereby increasing the possibility of macromolecular binding, resulting in pathological changes which could include tumors (ATSDR 1993). Data on the point at which saturation is reached is unclear according to ATSDR (1993).

Toxicity Values

Data by Tseng (1977) and Tseng et al. (1968) from a population epidemiology study in Taiwan were used to derive an ingestion RfD of 0.3 µg/kg-day (EPA 1998). The critical effects were considered to be hyperpigmentation, keratosis, and possible vascular complications. Since hyperpigmentation and keratosis of the skin are lesions that potentially may progress to skin neoplasms, this toxic endpoint is considered to be appropriate for RfD derivation. EPA has derived a RfD of 0.3

µg/kg-day. incorporating an additional uncertainty factor of 3 for the lack of data concerning the potential toxicity of arsenic and to for sensitive individuals.

A dermal reference dose does not exist and was derived by adjusting the oral reference dose by a 10% oral absorption adjustment factor (NCEA 1992). The derived dermal reference dose is 4 H 10^{-5}.

Considerable scientific controversy has surrounded the derivation of an estimated SF for arsenic by ingestion, principally drinking water. Based on a study in Taiwan (Tseng 1977; Tseng et al. 1968), EPA has developed an oral slope factor of 1.5 $(mg/kg\text{-}day)^{-1}$. The SF for ingestion was adopted in this risk assessment for skin contact, as a default condition (EPA 1998). The dermal slope factor was derived by adjusting the oral slope factor by a 95% oral absorption adjustment factor (NCEA 1992).

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BARIUM

Cancer

EPA (199) indicates that there are insufficient data for an assessment of the carcinogenicity of barium compounds. Similarly, ATSDR (1992) notes a lack of carcinogenicity studies via inhalation or dermal exposure routes, but summarizes two rodent studies (Schroeder and Mitchener 1975 a,b) that observed no significant differences in tumor incidence between treated and control animals. ATSDR, however, considers these rodent studies inadequate for evaluating the carcinogenic potential of barium due to insufficient numbers of animals, no determination of an MTD, only one exposure dose, incomplete histology, and an unspecified purity of the test material.

Mutagenicity

ATSDR (1992) summarizes that data are insufficient to support a conclusive statement regarding the genotoxicity of barium, due to an absence of *in vivo* genotoxicity studies and equivocal results from *in vitro* assays.

Toxicity

Exposures to barium via the oral route are used in the majority of studies evaluating potential toxicity. ATSDR (1992) indicates a variety of effects following sub-chronic or chronic oral administration of barium, including mortality, respiratory, cardiovascular, hematological, musculoskeletal, hepatic, renal, neurological, and other effects. For both subchronic (15B364 days) and chronic (>365 days) exposures, cardiovascular effects are the most sensitive endpoint. With subchronic exposures, rodent NOAELs for all systemic effects except cardiovascular are approximately 10 mg/kg-d. For cardiovascular effects, rat NOAELs are reported as low as 0.64B0.71 mg/kg-d (Perry *et al.* 1983, 1985, 1989) and the human NOAEL is reported as 0.21 mg/kg-d (Wones *et al.* 1990).

Studies identifying the adverse effects of sub-chronic or chronic barium exposure via inhalation are limited in their utility for linking adverse health effects with barium exposure (ATSDR 1992). Even with the limited utility of these studies, these studies suggest a potential association between non-acute barium inhalation exposures and respiratory, cardiovascular, hematological, hepatic, developmental, and reproductive effects (ATSDR 1992). According to EPA (1995):

> Occupational studies of workers exposed to barium dust have shown that workers develop "baritosis." Affected workers showed no symptoms, no abnormal physical signs, no loss of vital capacity or interference with function, although they had a significantly higher incidence of hypertension.

Toxicokinetics

In human beings, the absorption of barium from the gastrointestinal tract largely depends on age and the solubility of the compound. Less than 10% of an ingested quantity is believed to be absorbed in adults; however, absorption may be significantly higher in children. Inhaled barium compounds are absorbed through the lungs or directly from the basal membrane. Poorly soluble compounds may accumulate in the lungs and removal is slow. Absorbed barium enters the bloodstream and various soft tissues, and is deposited in the bone. Barium is eliminated in both the feces and the urine, elimination varying according to the route of administration and the solubility of the compound (WHO 1991).

Metabolism

The metabolism of barium is similar to that of calcium, another divalent cation, although barium has no known biological function (WHO 1991). Underwood (1971), however, indicates that barium may play an essential role for some organisms since rats and guinea pigs fed a barium-free diet fail to grow normally. Because of the molecular similarity between calcium and barium, barium may cycle through the same homeostatic processes as calcium, and barium would thereby exist in a physiological steady-state within a chronically-exposed organism. In cases of barium excess, homeostatic mechanisms may be overridden, and toxicity would ensue.

Toxicity Values

EPA (1998) has established an oral RfD for barium of 0.07 mg/kg-d based on increased blood pressure from subchronic and chronic human drinking water studies (Brenniman and Levy 1984; Wones *et al.* 1990) and other supporting rodent studies (Perry *et al.* 1983; McCauley *et al.* 1985; Schroeder and Mitchener 1975a,b; Tardiff *et al.* 1980). The uncertainty factor is modified from the default 10-fold values for the use of a subchronic study and for protection of sensitive individuals because EPA considers the critical study's unique focus and other supporting studies as supporting an uncertainty factor of 3.

A dermal RfD was estimated by adjusting the oral RfD by an oral absorption adjustment factor of 100% (NCEA 1993).

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BENZO(a)ANTHRACENE

Benzo(a)anthracene (BaA) ($C_{18}H_{12}$, MW 228.3, CAS registry number 56-55-3) is a polynuclear aromatic hydrocarbon that exists as solid, colorless plates with a greenish-yellow fluorescence at standard temperature and pressure. It occurs as a by-product of incomplete combustion of organic substances. It is a constituent in mainstream cigarette smoke, exhaust emissions from gasoline engines, charcoal-broiled foods, and crude oils.

Cancer

Benzo(a)anthracene is classified by EPA as a category B2, probable human carcinogen, based on no human data but sufficient data from animal bioassays.

There were no reported epidemiologic data in humans assessing the carcinogenicity of BaA, although BaA is a component of mixtures that have been associated with human cancer. These mixtures include coal tar, soots, coke oven emissions, and cigarette smoke (EPA 1995).

A group of male B6AF1/J mice was exposed by gavage to 3 percent solutions BaA in dioctyl ester of sodium sulfosuccinic acid three times per week for 5 weeks (total dosage was approximately 225 mg/mouse) (Klein 1963). On days 437B444 and 547 after treatment, mice were examined for tumor formation. There were increased incidences of pulmonary adenoma and hepatoma in treated animals versus controls at both observation times. The incidence of pulmonary adenoma at 437B444 days was 95 percent in treated animals versus 26 percent in controls, and at day 547 treated animals had an incidence of 95 percent versus 35 percent for controls. For hepatomas at 437B444 days, treated animals had an incidence of 46 percent versus 0 percent in controls, and at day 547, 100 percent hepatomas in treated animals versus 10 percent in controls. In another study, mice (strain and sex not specified) dosed with multiple gavage of 0.5 mg BaA in mineral oil (17 mg/kg for 8 or 16 treatments at 3B7 day intervals) resulted in forestomach papillomas in 2 out of 27 treated mice and none in controls (EPA 1995).

BaA yielded positive results in tests for complete carcinogenicity and initiating activity in skin painting assays in C3H/He, CAF1, and ICR/Ha mouse strains (EPA 1995). C3H/He mice were painted 3 times weekly with several concentrations (0.002 percent, 0.02 percent, 0.2 percent, or 1 percent) of BaA in toluene or in n-dodecane. Tumors, mostly malignant, formed after 50 weeks off treatment in the three lower concentrations (Bingham and Falk 1969).

Groups of male and female CD-1 mice received intraperitoneal injections of BaA in DMSO on days 1, 8, and 15 of age (total dosage 638 μg/mouse) (Wislocki et al. 1986). There was a statistically significant increase in the incidence of liver adenomas or carcinomas (31/39 in treated versus 2/28 in controls); however, female mice did not develop liver tumors. There was an increase in pulmonary adenomas or carcinomas in males (not statistically significant), although the incidence in female treated mice was increased significantly (6/32 in treated versus 0/31 in controls).

Subcutaneous injection of BaA in tricaprylin into C57B1 mice produced injection site sarcomas 9 months following treatment. The doses were 0.05, 0.2, 1.0, 5.0, or 10 mg, and the corresponding incidence of tumor formation was 12 percent, 26 percent, 48 percent, 34 percent, and 31 percent, respectively. A statistical analysis was not reported (EPA 1995).

Intramuscular injection of BaA in combination with 1 percent or 3 percent croton oil produced injection site fibrosarcomas and hemangioendotheliomas in Strain A-derived albino mice. Of the mice injected with BaA in 1 percent croton oil, 3/24 developed tumors, and in the 3 percent croton oil administration, 1/26 developed tumors.

Mutagenicity

BaA was mutagenic to *S. Typhimurium*, *Drosophila melanogaster*, and mammalian cell *in vitro* in the presence of an exogenous metabolic system. There was some evidence of clastogenic activity as BaA yielded mostly positive results for DNA damage, mutations, chromosomal effects, and cell transformation in a variety of eukaryotic cells (EPA 1995).

Toxicity

No studies were located that investigated the toxicity of BaA in either humans or animals.

Toxicokinetics

No studies have been located on the absorption of BaA in isolation, although BaA undergoes intestinal transport by passive diffusion (Rees et al. 1971). A discussion of the toxicokinetics of PAHs as a class of compounds is presented in the toxicity profile for acenapthene.

BaA is similar to other polynuclear aromatic hydrocarbons that have a Abay-region≅ structure and is metabolized by the mixed function oxidases to reactive Abay-region≅ diol epoxides (i.e., the sterically hindered cup-shaped area between carbons 1 and 12 of benzo(a)anthracene). Intermediates of diol epoxide are currently considered to be the ultimate carcinogen for alternant PAHs (Jerina et al. 1980). These diol epoxides are easily converted into carbonium ions, which are alkylating agents. BaA is metabolized to all five of its dihydrodiols and a number of phenolic metabolites and conjugates. The 3,4-dihydrodiol is mutagenic in the presence of rat liver microsomal fraction, and the 3,4-dihydrodiol and 3,4-diol-1,2-epoxide are also highly tumorigenic.

Toxicity Values

The relative potency factor for BaA is 0.1 (EPA 1993). This toxicity equivalency factor is used in conjunction with the SF for benzo(a)pyrene (7.3 $(mg/kg\text{-}d)^{-1}$) to estimate cancer risks to BaA via oral exposures only. Inhalation and dermal cacner risks cannot be estimated for BaA (EPA 1993). No reference dose is available for BaA (EPA 1998).

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BENZO(a)PYRENE

Benzo(a)pyrene ($C_{20}H_{12}$, MW 252.3, CAS registry number 50-32-8) is the most extensively studied of the PAHs. Benzo(a)pyrene (BaP) is the most toxic PAH to animals and has the highest carcinogenic potency. In its pure physical state, BaP is in the form of pale yellow needles and is virtually insoluble in water. It is sparingly soluble in ethanol and methanol, and soluble in benzene, toluene, and xylene. BaP undergoes photooxidation with indoor sunlight or fluorescent light in organic solvents, and oxidatively reacts with ozone. It readily undergoes nitration and halogenation (Clar 1964), and reacts with nitrous oxide and nitrogen dioxide in the environment to form nitro derivatives (Butler and Crossley 1981). Benzo(a)pyrene is formed by the incomplete combustion of coal, oil, and gas, and is also a constituent of fossil fuels. It has been identified in cigarette smoke, air of restaurants, engine exhaust, motor oils, margarine, butter, roasted coffee, and numerous water bodies.

Cancer

BaP has been classified as a probable human carcinogen (category B2) by EPA (1998).

There have been no studies located regarding cancer in humans following inhalation of BaP only. However, epidemiologic studies have demonstrated increased mortality due to lung cancer in humans exposed via inhalation to coke-oven emissions (Lloyd 1971; Mazumdar et al. 1975; Redmond et al. 1976), roofing-tar emissions (Hammond et al. 1976), and cigarette smoke (McLure and MacMahon 1980), all of which contain BaP. Reports of skin tumors among individuals exposed to mixtures containing BaP have also been documented. The earliest of these is the report by Pott (1775) of scrotal cancer among chimney sweeps. More recently, skin cancer among humans dermally exposed to shale oils has been reported (Purde and Etlin 1980). In addition to BaP, each of these mixtures contains other PAHs including chrysene, benzo(a)anthracene, benzo(b)fluoranthene, and dibenzo(a,h)anthracene, as well as other potentially carcinogenic chemicals, including nitrosamines, coal tar pitch, creosote, and other PAHs. It is impossible to evaluate the contribution of any individual PAH to the total carcinogenicity of these mixtures in human studies because of the complexity of the mixtures and the presence of other carcinogens. Therefore, epidemiologic evidence in humans regarding the potential carcinogenicity of BaP is inadequate.

Dietary, gavage, inhalation, intratracheal instillation, dermal, and subcutaneous studies in numerous strains of at least four species of rodents and several primates have been performed with BaP. Repeated BaP administration has been associated with increased incidences of total tumors and of tumors at the site of exposure. Distant site tumors have also been observed after BaP administration by various routes. BaP is frequently used as a positive control in animal carcinogenicity bioassays. These studies are described below.

In a chronic inhalation study, hamsters were exposed to 9.5 mg/m^3 and 46.5 mg/m^3 of inhaled BaP for 109 weeks (Thyssen et al. 1981). Approximately 99 percent of BaP particles were between 0.2 and 0.54 microns in diameter (i.e., small enough to deposit deeply in the lung). Respiratory tract tumors were induced in the nasal cavity, pharynx, larynx, and trachea in a dose-related manner. However, no lung tumors were observed. Papillary polyps and squamous cell papillomas and carcinomas were also induced in the esophagus and forestomach of animals in the high dose group, presumably as a consequence of mucociliary particle clearance and swallowing of particles.

BaP administered via inhalation at a dose of 10 mg/m^3 to rats exposed simultaneously to sulfur dioxide (Laskin et al. 1970) increased the incidence of squamous cell lung carcinomas as compared with the incidence observed when BaP was administered alone. Sulfur dioxide, by itself, is not known to be carcinogenic (NRC 1978). This study indicates that carcinogenicity resulting from high doses of BaP can be enhanced with concurrent inhalation exposure to other environmental gases.

BaP administered in the diet or by gavage to mice, rats, and hamsters has produced an increased incidence of stomach tumors. In a study by Neal and Rigdon (1967), BaP was administered to mice in the diet at the following ppm concentrations: 0, 1, 10, 20, 30, 40, 45, 50, 100 and 250. At the

three highest doses, statistically significant, dose-related forestomach tumors were produced. Brune et al. (1981) administered 0.15 mg/kg (body weight) of BaP in the diet to Sprague-Dawley rats either every 9th day or 5 times/week. These treatments resulted in annual average doses of 6 or 39 mg/kg, respectively. Combined incidences of tumors of the forestomach, esophagus, and larynx showed a statistically significant increase that was dose-related. As part of the same study, Brune et al. (1981) administered 0.15 mg/kg of BaP to groups of Sprague-Dawley rats via caffeine gavage at the following dose rates: every 9th day, every 3rd day, or 5 times per week. These treatments resulted in annual average doses of 6, 18, or 38 mg/kg, respectively. A high level of mortality occurred in the high dose group. There was a statistically significant association between dose and the proportions of rats with combined tumors of the forestomach, esophagus, and larynx.

A statistically significant increase in mammary tumors has also been observed following eight weekly oral doses of 12.5 mg/kg BaP, administered to female rats for 90 weeks (McCormick 1981).

Topical application of BaP was first reported in 1933 to induce skin tumors in mice (Cook et al. 1933). Studies by Wynder and Hoffman (1959a) and Wynder and Ritz (1957) have shown that mice receiving 0.001-0.01 percent of BaP applied dermally to their shaved backs throughout their lifetime exhibited a dose-related increase in squamous cell papillomas and carcinomas. Other studies have supported the finding that dermal application of BaP increases the incidences of both benign and malignant skin tumors: mice treated topically throughout their life span with doses of BaP ranging from 2 to 12.5 µg/day developed increased incidences of squamous cell papillomas and carcinomas (Habs et al. 1984; Warshawsky and Barkley 1987).

BaP is commonly used as a positive control in many dermal application bioassays and has been shown to cause skin tumors in other mammalian species, including rats, rabbits, and guinea pigs (EPA 1998). Some studies have also reported an increase in the incidence of tumors distant from the site of topical application (EPA 1991). Since a single dose of BaP was administered in many of these studies (EPA 1998), these data are not suitable for dose-response quantification.

Intratracheal instillation in guinea pigs, hamsters, and rats has resulted in elevated incidences of respiratory tract tumors (EPA 1991). Intraperitoneal BaP injections have caused increases in the number of injection site tumors in rats and mice (EPA 1991). Subcutaneous BaP injections have caused increases in the number of injection site tumors in mice, rats, guinea pigs, hamsters, and some primates (IARC 1983; EPA 1991). BaP has also been reported to be carcinogenic in animals when administered by the following routes: intravenously; by implantation in the stomach, lung, kidney or brain; and transplacentally, following intraperitoneal injection of pregnant rats (EPA 1998).

Mutagenicity

BaP is mutagenic in the Ames assay and in prokaryote and mammalian cell culture tests for DNA damage (EPA 1991). Genotoxic effects have also been observed when BaP has been tested for chromosomal damage (e.g., sister chromatid exchange and chromosomal aberration) and cell transformation (IARC 1983).

Toxicity

General systemic toxicity effects resulting from administration of high doses of BaP to animals are typically mild (ATSDR 1990). Most of these effects involve changes in enzyme levels and/or organ weights. In rats, acute intragastric administration of 150 mg/kg-day of BaP resulted in suppressed carboxylesterase activity in the intestinal mucosa (Nousiainen et al. 1984). Following a diet containing 2-acetylaminofluorene and carbon tetrachloride, a single intragastric BaP administration of 200 mg/kg to partially hepatectomized rats induced preneoplastic hepatocyte foci, also known as gamma glutamyl transpeptidase foci, in the liver (Tsuda and Farber 1980). BaP was the most potent foci inducer among several PAHs tested. Rats intragastrically administered 100 mg/kg-day of BaP for 4 days exhibited induction of cytosolic aldehyde dehydrogenase, a liver enzyme (Torronen et al. 1981). BaP also induced carboxylesterase activity in the liver (Nousiainen et al. 1984). In another study, partially hepatectomized rats fed a diet containing 51.4 mg/kg-day of BaP showed statistically significant increases in the extent of liver regeneration, which is indicative of the ability to induce a proliferative cell response (Gershbein 1975). In the kidney, microsomal carboxylesterase activity of rats was moderately induced by 50B150 mg/kg of BaP administered intragastrically (Nousiainen et al. 1984).

Two studies have demonstrated developmental effects of BaP exposure on inbred rats and mice. In a study by MacKenzie and Angevine (1981), BaP was administered by gavage to pregnant mice at doses of 10, 40, and 160 mg/kg-day. Mean pup weight was significantly reduced in all treatment groups and the viability of litters at parturition was significantly decreased in the highest dose group. When these pups (F_1 progeny) were bred with untreated animals, the F_1 animals exposed *in utero* to the two highest doses were sterile, while the F_1 progeny from the low dose maternal exposure group showed decreased fertility with associated alterations in gonadal morphology and germ-cell development. In another study by Shevaleva (1978), decreased maternal weight gain and hematological changes were reported in pregnant rats administered BaP daily during gestation. Additional effects included: dose-related increases in pre- and post-implantation losses; decreased fetal survival; and reduced fetal weights. Hydronephrosis and bladder dilation were reported in fetuses at all dose levels. A study by Rigdon and Neal (1965) reported no adverse developmental effects when BaP was administered in the diet to mice at concentrations equivalent to 33.3, 66.7, or 133.3 mg/kg-day at varying times before and after mating. This study, however, is difficult to evaluate because BaP administration protocols were inconsistent, and thus maternal doses varied within treatment groups.

Two studies in mice (MacKenzie and Angevine 1981; Rigdon and Neal 1965) and one in rats (Rigdon and Rennels 1964) demonstrated that BaP administration at high doses induced reproductive toxicity in rodents. As discussed in the previous section on developmental toxicity, BaP administered by gavage to pregnant CD-1 mice decreased the percentage of females who successfully completed their pregnancies and produced a high incidence of sterility in the progeny (MacKenzie and Angevine 1981). In contrast to these findings, BaP administered in the diet to pregnant Swiss mice caused no adverse effects on fertility (Rigdon and Neal 1965), but reduced the incidence of pregnancy in rats (Rigdon and Rennels 1964).

BaP is immunogenic when applied dermally to the skin of C3H mice. In a study by Klemme et al. (1987), acute topical application of 120 µg BaP elicited an allergic contact hypersensitivity which was antigen-specific.

Toxicokinetics

Although little data are available regarding the absorption of PAHs, including BaP, in humans following inhalation exposure, absorption of PAHs can be inferred from the presence of urinary metabolites of PAHs in workers occupationally exposed to these compounds (Becher and Bjorseth 1983). Experimental data from a skin penetration and metabolism study of topically applied BaP to skin samples from six mammalian species, including humans, showed that metabolic viability was a major factor involved in the *in vitro* skin permeation (Kao et al. 1985). The extent of skin permeation after 24 hours was established as 3 percent of an applied dose of BaP (10 µg/cm^2). Results from the Kao et al. (1985) study show that diffusion and metabolism are also involved in the percutaneous fate of surface-applied BaP; permeation was accompanied by extensive Afirst-pass≅ metabolism. The high occupational concentration of PAHs, however, did not correspond to the amount of PAHs deposited, metabolized, and excreted in this study. The authors suggest that PAHs adsorbed to airborne particulate matter may not be bioavailable and that the dose-uptake relationship may not be linear over the entire PAH concentration range. Indirect evidence also suggests that BaP may not be readily absorbed following ingestion in humans (Hecht et al. 1979), but is readily absorbed following oral administration in the rat (Yamazaki et al. 1987). Intestinal absorption of PAHs appears to be highly dependent on the presence of bile in the stomach (Rahman et al. 1986). Application of 2 percent crude coal tar to the skin of humans for 8-hour periods on 2 consecutive days showed evidence of absorption of pyrene as well as other non-carcinogenic PAHs (Storer et al. 1984).

The lipophilicity of PAHs enables them to readily penetrate cellular membranes and remain in the body indefinitely; however, the metabolism of PAHs alters these chemical compounds both structurally and chemically, and renders them more water-soluble, and, hence more excretable. Metabolism of PAHs occurs in all tissues. PAHs are biotransformed to chemically reactive intermediates that covalently bind to cellular macromolecules (i.e., DNA), leading to possible mutation and tumor initiation. Metabolites of PAHs include epoxide intermediates, dihydrodiols, phenols, quinones, and their various combinations. The Abay-region≅ (i.e., the sterically hindered cup-shaped area between carbons 10 and 11 of BaP) intermediates of diol epoxides are currently considered to be the ultimate carcinogen for alternant PAHs (Jerina et al. 1980). These diol epoxides are easily converted into carbonium ions, which are alkylating agents.

BaP is metabolized by the mixed function oxidase system, which includes microsomal cytochrome P-450 enzymes, to several arene oxides. Arene oxides may nonenzymatically rearrange to phenol, undergo hydration to trans-dihydrodiols in a reaction catalyzed by microsomal epoxide hydrolase, or react covalently with glutathione (GSH) spontaneously or in a reaction catalyzed by cytosolic GSH-S-transferase. Phenols may also be formed via P-450 enzymes by direct oxygen insertion, although the mechanism has not been unequivocally proven. 6-Hydroxybenzo(a)pyrene (6-HO-BaP) is further oxidized either spontaneously or metabolically by the enzyme prostaglandin endoperoxide

synthetase to the 1,6-, 3,6-, or 6,12-quinones (Panthanickal and Marnett 1981). There is evidence of further oxidation of two additional phenols, 3-HO-BaP to 3,6-quinone and 9-HO-BaP to the K-region 4,5-oxide. The phenols, quinones, and dihydrodiols are then conjugated to more water-soluble GSH conjugates and glucuronides and sulfate esters.

The dihydrodiols can undergo further oxidation, as opposed to conjugation. Cytochrome P-450 further oxidizes the 4,5-dihydrodiol to several uncharacterized metabolites and the 9,10-dihydrodiol to its 1- and/or 3-phenol derivative, with minor formation of 9,10-dihydrodiol-7,8-epoxide. The BaP-7,8-dihydrodiol is metabolized to a 7,8-dihydrodiol-9,10-epoxide, which is presently considered to be an ultimate carcinogenic metabolite, and a minor amount of phenol-diol formation. The diol epoxides can be conjugated with either GSH spontaneously or via GSH-S-transferase enzymatic reaction. Diol epoxides can also hydrolyze spontaneously to tetraols.

The metabolism of BaP has been demonstrated in *in vitro* studies using human bronchial epithelial and lung tissue (Autrup et al. 1978; Cohen et al. 1976; Kiefer et al. 1988) and human hepatocytes (Diamond et al. 1980; Monteith et al. 1987), and numerous *in vivo* animal studies (Bassett et al. 1988; Dahl et al. 1985; Bond et al. 1988; Fiume et al. 1983). The route by which PAHs enter the body may effect their metabolism and excretion. Inhalation of PAHs may bypass the first-pass effect of the liver that is seen after oral exposures. Enzyme activity among tissues are variable and may subsequently alter the degree of bioavailability of the PAHs. Specific enzymes, induced by exposure to BaP, are believed to be responsible for the metabolism of BaP and other PAHs (e.g., aryl hydrocarbon hydroxylase). While some enzymatic activities are enhanced, other pathways may be suppressed (Jacob et al. 1983). For a review of BaP metabolism, see DePierre and Ernster (1978) and Pelkonen and Nebert (1982).

No studies have been found on the excretion of PAHs following inhalation, oral, or dermal exposure. Studies on the excretion of BaP in animals, however, have been characterized. The excretion of BaP in a mouse following a single intratracheal instillation of tritiated BaP (i.e., [^{3}H]-BaP) cleared rapidly with a half life ($T_{1/2}$) of approximately 8 hours. After 24 hours, about 85 percent of the dosed BaP was cleared form the lung (Schnizlein et al. 1987). Rats also exhibited rapid clearance of BaP from inhalation, with 40 percent cleared within 5 minutes and >94 percent of the dose eliminated from the lung after 6 hours after exposure (Weyand and Bevan 1988). A large fraction of administered BaP after intratracheal instillation was excreted in the bile (Weyand and Bevan 1986, 1988), and the rate of BaP excretion into bile declined as the dose increased in rats and guinea pigs. Metabolites excreted in the bile included thioether conjugates (62.5 percent), glucuronide conjugates (22.8 percent), sulfate conjugates (7.4 percent), and free BaP (9.8 percent) (Weyand and Bevan 1988). Intravenous administration of 0.001 mg/kg BaP fit a triexponential model, similar to inhalation exposure (i.e., intratracheal instillation), with $T_{1/2}$s of 1.5, 22.4, and 178 minutes (Weyand and Bevan 1986).

Toxicity Values

Carcinogenic PAHs appear to exert their effects mainly at the point of contact (dermal application results in skin tumors), or portal of entry (ingestion results mainly in forestomach tumors; inhalation results in respiratory tract tumors and tumors of the upper digestive tract X presumably due to mucociliary particle clearance and involuntary ingestion of particles). Tumors distant from the point of application have also been observed.

Among the PAHs, seven have the ability to elicit cancer: benzo(a)pyrene, benzo(a)anthracene, benzo(b)fluoranthene, benzo(k)fluoranthene, dibenzo(a,h,)anthracene, indeno(1,2,3-cd)pyrene, and chrysene. BaP is the most potent carcinogenic among the PAHs.

For ingestion and skin contact of BaP, a SF of 7.3 $(mg/kg\text{-}day)^{-1}$ has been promulgated by EPA (1998). This SF is the geometric mean of several slopes (ranging from 4.5 to 11.7 $[mg/kg\text{-}day]^{-1}$) from the studies of Neal and Rigdon (1967) and of Brune et al. (1981).

Few studies have evaluated the carcinogenic effects of inhalation exposure to BaP or other PAHs. Rats exposed chronically to combustion gases of a coal-burning furnace enriched with BaP developed lung tumors; however, these gases contained other PAHs, as well as other potentially carcinogenic compounds, so that a direct association between BaP exposure and lung tumors cannot be made (Heinrich et al. 1986).

For each of the other six carcinogenic PAHs, no adequate human or animal data exist to directly estimate a SF. EPA Region I methodology involves the utilization of BaP=s SF for the other carcinogenic PAHs, along with a conversion of the measured concentrations of each carcinogenic PAH to an Aequivalent≅ concentration of benzo(a)pyrene, according to the following table (EPA 1993):

Compound Relative Potency Value	
Benzo(a)anthracene	0.1
Benzo(b)fluoranthene	0.1
Benzo(k)fluoranthene	0.01
Benzo(a)pyrene	1.0
Chrysene	0.001
Dibenzo(a,h)anthracene	1.0
Indeno(1,2,3-cd)pyrene	0.1

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BENZO(b)FLUORANTHENE

Benzo(b)fluoranthene ($C_{20}H_{12}$, MW 252.3, CAS registry number 205-99-2) is a polynuclear aromatic hydrocarbon that exists in pure form as colorless needles. Benzo(b)fluoranthene (BbF) is virtually insoluble in water, and slightly soluble in organic media. BbF occurs in fossil fuels, and is formed by the incomplete combustion of fossil fuels. It has also been identified in cigarette smoke, engine exhaust, broiled and smoked food, edible oils and margarines, and various water bodies.

Cancer

Benzo(b)fluoranthene is classified by EPA as a category B2, probable human carcinogen, based on no human data but sufficient data from animal bioassays.

Epidemiologic studies have demonstrated increased mortality due to lung cancer in humans exposed via inhalation to coke-oven emissions (Lloyd 1971; Mazumdar et al. 1975; Redmond et al. 1976), roofing-tar emissions (Hammond et al. 1976), and cigarette smoke (McLure and MacMahon 1980). Reports of skin tumors among individuals exposed to mixtures containing BbF have been documented. The earliest of these is the report by Pott (1775) of scrotal cancer among chimney sweeps. More recently, skin cancer among humans dermally exposed to shale oils has been reported (Purde and Etlin 1980). Each of these mixtures contains a number of PAHs, including benzo(a)pyrene, benzo(b)fluoranthene, chrysene, benzo(a)anthracene, benzo(k)fluoranthene, and dibenzo(a,h)anthracene, as well as other potentially carcinogenic PAHs and other potentially carcinogenic chemicals, including nitrosamines, coal tar pitch, and creosote. It is impossible to evaluate the contribution of any individual PAH to the total carcinogenicity of these mixtures in humans because of the complexity of the mixtures and the presence of other carcinogens. Therefore, epidemiologic evidence in humans regarding the potential carcinogenicity of BbF is inadequate.

A dose-response relationship for the dermal carcinogenicity of BbF has been demonstrated over an order-of-magnitude dose range in Swiss mice receiving daily topical doses throughout their lifetime (Wynder and Hoffmann 1959b). Survival was also dose-dependent. The time-to-tumor latency was short, with skin papillomas and carcinomas appearing in high dose groups after 5 months of treatment.

Mutagenicity

A single topical application of 100 µg BbF was reported to bind to DNA in mouse skin (Weyand et al. 1987). The relative extent of binding for carcinogenic PAHs was benzo(b)fluoranthene > benzo(k)fluoranthene > indeno(1,2,3-cd)pyrene (Weyand et al. 1987), which corresponds to the relative cancer potency of these PAHs.

Toxicity

No animal studies were located that assessed the systemic, developmental, reproductive or other toxicity of BbF.

Toxicokinetics

PAHs have been divided into two groups, based on structural similarity and likely metabolic/detoxification pathways. These two groups have been termed Aalternant≅ and Anon-alternant≅ and differ in the electron density associated with the molecule. Alternant PAHs have an equally distributed electron density, whereas non-alternant PAHs have an uneven distribution of electron density from one portion of the molecule to the other and behave almost as if they were two

different molecules. Structurally, alternant PAHs consist of multiple 6-membered rings, whereas non-alternant PAHs consist of several 6-membered rings, and one 5-membered ring to which many of the 6-membered rings are attached. It is the 5-membered ring that contributes substantially to the uneven distribution of electron density. Generally, alternant PAHs are more potent than non-alternant PAHs (ATSDR 1990b), and the mechanisms of carcinogenicity appear to be different between the two groups. BbF is a non-alternant PAH.

The mechanism of carcinogenicity of non-alternant PAHs is unclear, because non-alternant PAHs either do not have a bay region or have been shown not to be activated via a bay-region epoxide, as are alternant PAHs (Amin et al. 1985a,b). Studies of BbF metabolism indicate the major metabolites of this non-alternant PAH are 6-hydroxybenzo(b)fluoranthene and 4- or 7-hydroxybenzo(b)-fluoranthene; the predominant diol formed was trans-11,12-dihydro-11,12-dihydroxy-benzo(b)-fluoranthene (Amin et al. 1982, 1985b). There was no evidence to suggest that a diol epoxide is the ultimate carcinogenic metabolite of non-alternant PAHs. If non-alternants differ in their mechanism of action, then they may also differ with regard to other factors, including target organ and species sensitivity.

Toxicity Values

The relative potency factor for BbF is 0.1 (EPA 1993). This toxicity equivalency factor is used in conjunction with the SF for benzo(a)pyrene (7.3 $(mg/kg\text{-}d)^{-1}$) to estimate cancer risks to BbF via oral exposures only. Inhalation and dermal cacner risks cannot be estimated for BbF (EPA 1998). No reference dose is available for BbF (EPA 1998).

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Cadmium

The U.S. EPA (1998 has classified cadmium (Cd) as a probable human carcinogen (Category B1). The inhalation of cadmium has been shown to produce respiratory tract cancers in humans and various tumors in rats and mice following inhalation and injection exposures. No positive cancer studies of ingested cadmium suitable for quantitation are available (U.S. EPA 1998).

Ingestion of cadmium results in nausea, vomiting, and abdominal pain. Inhalation of cadmium fumes may result in an acute chemical pneumonitis and pulmonary edema (Goyer 1986). The critical effects associated with chronic ingestion of cadmium are proteinuria and adrenal damage in humans.

The U.S. EPA (1998) has established oral RfDs of $5H10^{-4}$ mg/kg-day for cadmium in drinking water and $1H10^{-3}$ mg/kg-day for cadmium in food. For both exposure media, the critical effect was significant proteinuria in human subjects chronically exposed to cadmium. Both RfDs were also based on an aggregate uncertainty factor of 10, to account for intra-human variability to the toxicity of this compound in the absence of specific data on sensitive individuals. The RfD is based on the highest level of cadmium in the human renal cortex not associated with significant proteinuria, with modeled exposures adjusted to allow for absorption differences arising from differing cadmium sources (U.S. EPA 1998).

An inhalation RfD is pending verification (U.S. EPA 1998). Accordingly, the oral RfD for cadmium in water was used as the surrogate for inhalation. The oral RfD is $1H10^{-3}$ mg/kg-day (USEPA 1998). The dermal RfD does not exist and was estimated by adjusting the oral RfD by an oral absorption adjustment factor of 2.5% (USEPA 1998).

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CHLORDANE

Cancer

Chlordane is classified by EPA (1998) as a Category B2, probable human, carcinogen based on sufficient evidence in studies in which benign and malignant liver tumors were induced in four strains of mice of both sexes and in F344 male rats (Becker and Sell 1979; Velsicol 1973; NCI 1977; Velsicol 1983a,b; Ingle 1952; Ambrose et al. 1953a,b). Chlordane is also structurally related to other liver carcinogens. (EPA 1998).

EPA (1998) discussed three epidemiologic studies of workers exposed to chlordane and/or heptachlor. One study of pesticide applicators was considered inadequate in sample size and

duration of follow-up. This study showed marginal statistically significant increased mortality from bladder cancer (3 observed) (Wang and McMahon 1979a). The other two studies (Wang and McMahon 1979b; Ditraglia et al. 1981) were of pesticide manufacturing workers. Neither of these studies showed any statistically significantly increased cancer mortality and both of the populations had confounding exposures from other chemicals.

Dose-related incidences of liver carcinoma constitute the major finding in mice. Becker and Sell (1979) tested chlordane (90:10 mixture of chlordane to heptachlor) in C57B1/6N mice at 0, 25 and 50 ppm (0, 3.57, 7.14 mg/kg bw) for 18 months. Twenty-seven percent of the surviving treated mice developed primary hepatocellular carcinomas, and none of the controls developed tumors or nodular lesions of the liver. Velsicol (1973) fed groups of male and female CD-1 mice diets with 0, 5, 25 or 50 ppm analytical grade chlordane for 18 months. A significant dose-related increase in nodular hyperplasias in the liver of male and female mice was reported at the the two highest dose levels. A dose-related increase of hepatocellular carcinomas was also observed in both sexes of B6C3F1 mice (NCI 1977). Male and female mice were fed technical-grade chlordane at concentrations of 29.9 and 56.2 ppm and 30.1 and 63.8 ppm, respectively, for 80 weeks. ICR male mice developed hepatocellular adenomas and hemangiomas when fed 12.5 ppm chlordane for 24 months (Velsicol 1983a). No tumors were observed in the female mice when tested at the same concentrations (Velsicol 1983a).

Velsicol (1983b) reported a long-term (130 weeks) carcinogenesis bioassay on 80 male and 80 female F344 rats fed concentrations of 0, 1, 5, and 25 ppm chlordane. A significant increase in adenomas of the liver was observed in male rats receiving 25 ppm. Although no tumors were observed in female rats, hepatocellular swelling was significantly increased at 25 ppm. NCI (1977) reported a significant increase of neoplastic nodules of the liver in low-dose Osborne-Mendel female rats (120.8 ppm) but not in the high-dose group (241.5 ppm). No tumor incidence was reported for the males fed at 203.5 and 407 ppm. Loss of body weight and a dose-related increase in mortality was observed in all treated groups. High mortality and reduced growth rates in Osborne-Mendel rats was also observed by Ingle (1952) when the rats were exposed to 150 and 300 ppm chlordane, but not at 5, 10, and 30 ppm. No treatment-related incidence of tumors was reported. Significantly enlarged livers and liver lesions were found in male and female albino rats fed chlordane at greater than or equal to 80 ppm (Ambrose et al. 1953a,b). No treatment-related increase in tumors was found, but the 400 day study duration was short.

Mutagenicity

Gene mutation assays indicate that chlordane is not mutagenic in bacteria (Wildeman and Nazar 1982; Probst et al. 1981; Gentile et al. 1982). Positive results have been reported in Chinese hamster lung V79 cells and mouse lymphoma L5178Y cells with and without exogenous metabolism, as well as in plant assays. Chlordane did not induce DNA repair in bacteria, rodent hepatocytes (Maslansky and Williams 1981), or human lymphoid cells (Sobti et al. 1983). It is a genotoxicant in yeast (Gentile et al. 1982; Chambers and Dutta 1976), human fibroblasts (Ahmed et al. 1977), and fish (Vigfusson et al. 1983).

Toxicity

Charles River Fischer 344 rats (80/sex/dose) were fed technical chlordane at dietary levels of 0, 1, 5, and 25 ppm for 130 weeks (Velsicol 1983a). Body weight, food consumption, and water uptake were monitored at regular intervals. Clinical laboratory studies were performed and organ weights measured on eight animals/sex/group at weeks 26 and 52, and on all survivors at week 130. Gross and microscopic pathology were performed on all tissues. Daily dose level of 0.045, 0.229, and 1.175 mg/kg/day for males and 0.055, 0.273, and 1.409 mg/kg/day for females for the 1, 5, and 25 ppm treatment groups, respectively, were calculated from food consumption and body weight data. Regional liver hypertrophy in female rats was identified as the critical effect in this study (EPA 1998).

Studies of chronic and subchronic oral exposures in animals indicate that effects of chlordane exposure occur primarily on hepatic and neurological systems, with some reproductive, immunological, cardiovascular and renal effects. Liver effects are not severe, and include elevated serum liver enzymes, some tissue degeneration and cellualr enlargement. Neurological effects include some behavioral alterations, as well as tremors and irritability, with convulsions at higher doses (ATSDR 1992).

Limited to no information on effects following chronic and subchronic inhalation in animals or humans was found. Acute effects on occupationally exposed humans (production workers) included primarily neurological effects such as headaches, dizziness, nausea, muscle spasms, and sometimes convulsions. Due to difficulty in describing effects limited to solely dermal exposure, versus inhalation exposure, effects are deemed similar (ATSDR 1992).

Toxicokinetics

Chlordane is rapidly absorbed after oral or inhalation exposure, and shows affinity for fatty tissues. It can bioaccumulate following distribution to fat depots, liver, kidney, and brain (ATSDR 1992).

Metabolism

The two isomers of chlordane (cis and trans) are metabolized via different pathways, although the end result is a series of compounds with enhanced water solubility, for ease in excretion. Chlordane is capable of inducing its own metabolism, thereby aiding in excretion, but also aiding in the formation of toxic intermediaries. The cis isomer appears to be eliminated more rapidly than the trans isomer (ATSDR 1992).

Toxicity Values

EPA (1998) has established an oral RfD for chlordane of $H10^{-4}$ mg/kg-d based on liver cellular hypertrophy (with vacuolization) in animal studies as reported by Velsicol (1983a). The oral RfD was used as a surrogate for the dermal RfD.

EPA (1998) has established an oral SF for chlordane of 0.35 $(mg/k\ g\text{-}d)^{-1}$ based on hepatocellular carcinomas observed in mice and rats in long term feeding studies as reported by Velsicol (1973) and (NCI) 1977. The dermal slope factor was estimated by adjusting the oral SF by 80% (ATSDR 1994).

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CHROMIUM

Chromium (Cr, MW 52.0, CAS registry number 7440-47-3). Chromium is a metal that is found in varying oxidative states ranging from chromium(-II) to chromium(+VI). Cr^{2+} is the most commonly occurring natural form of the metal. Cr^{6+}, which originates strictly from anthropogenic sources, is of greatest toxicological significance. Chromium is produced from the reduction of chromite ore using carbon. Chromium in various forms is used in the metallurgic industry (alloys including stainless steel), the ceramics industry (granular chromite), and the chemical industry (pigments, plating, leather treatment, wood preservatives).

Cancer

Hexavalent chromium (Cr^{6+}) is classified as a human carcinogen by the EPA (category A), for the inhalation route, based on the demonstration by epidemiologic studies of an increase in the incidence of lung cancer in chromium-exposed workers (EPA 1998). For the oral route, hexavalent chromium can not be determined and thus, is classified in Group D (EPA 1998). There are a sufficient number of these studies to establish a dose-response relationship between chromium exposure and human lung cancer. These findings, however, may be confounded by the smoking habits of workers. In calculating the dose-response relationship, it was assumed by both the author of the studies (Mancuso 1975) and EPA (1995a) that the smoking rate among workers was similar to that of white males in the general U.S. population. However, several other epidemiologic studies on the distribution of smoking among human population groups suggest that the smoking rate may be higher among industrial workers than in the general population (EPA 1995a). Chromium workers are exposed to both trivalent and hexavalent chromium; however, only hexavalent chromium has been found to be carcinogenic in animal studies and only hexavalent chromium is considered to be a human carcinogen (EPA 1995a). When assessing carcinogenicity among workers, it has been assumed that the ratio of trivalent to hexavalent chromium is 6:1 (EPA 1995a).

Animal carcinogenicity studies with Cr^{6+} have supported the human evidence of carcinogenicity, producing the following tumors types: intramuscular injection site tumors in rats and mice; intrapleural implant site tumors for various hexavalent compounds in rats; intrabronchial implantation site tumors for various hexavalent compounds in rats; and subcutaneous injection site sarcomas in rats (EPA 1995a).

Mutagenicity

In general, hexavalent chromium is mutagenic in bacterial and yeast assays and in Chinese hamster ovary cells, whereas trivalent chromium is not (EPA 1995a). Chromosomal effects, unscheduled DNA synthesis and transformation of cell lines have been induced by exposure to various chromium compounds (Raffetto et al. 1977; Casto et al. 1979; Levis et al. 1978).

Toxicity

Other than localized pre-neoplastic histopathological changes in the lung, chromium does not appear to induce systemic toxicity. A 1-year drinking-water study in rats (MacKenzie et al. 1958) showed no systemic effects related to chromium exposure. Similarly, no toxicologically significant effects were observed in a 4-year study with dogs (Anwar et al. 1961), or in a group of humans who drank water for 3 years from a private well containing chromium concentrations of 1 mg/L (EPA 1995a).

No studies have been documented examining the possible developmental or reproductive effects resulting from ingestion of chromium.

Toxicokinetics

Absorption of inhaled chromium compounds depends on several factors, including physical and chemical properties of the particles, such as oxidation state, size, and solubility, and the activity of alveolar macrophages (ATSDR 1991c). The identification of chromium in urine and serum of humans occupationally exposed to soluble trivalent or hexavalent compounds in air indicates that chromium can be absorbed from the lungs (Randall and Gibson 1987); hexavalent chromium compounds appear to be more readily absorbed from the lungs than trivalent compounds, due in part to differences in the capacity to penetrate biological membranes. Chromium is also absorbed through the gastrointestinal tract, but at a much lower rate than through the lungs (ATSDR 1993). The absorption efficiency depends on the dietary intake (Anderson 1986). Both trivalent and pentavalent chromium can penetrate human skin to some extent (Samitz and Shrager 1966).

Metabolically, trivalent chromium compounds are essential to normal glucose, protein, and fat metabolism (Anderson 1986). In the lung, hexavalent chromium can be reduced to trivalent chromium by ascorbate. This reduction results in a shorter residence time of chromium in the lungs and constitutes the first defense against oxidizing reagents in the lung (Suzuki and Fukuda 1990). When ascorbate is depleted from the lungs, hexavalent chromium can also be reduced by glutathione, although this is a slower process than reduction by ascorbate (Suzuki and Fukuda 1990). Uptake and reduction of chromium compounds by pulmonary macrophages also occurs and appears to constitute a second line of defense against the pulmonary toxicity of hexavalent chromium compounds (Petrilli et al. 1986). The reduction of hexavalent chromium to trivalent chromium in cell extracts made from human pulmonary alveolar macrophages significantly reduces the mutagenic potency of chromium when it is tested in the Ames *Salmonella* assay (Petrilli et al. 1986).

Hexavalent chromium may also be reduced to trivalent chromium by ascorbate in the gastrointestinal tract when exposure is oral (Samitz 1970). Reduction of hexavalent chromium may also result in the formation of pentavalent chromium (ATSDR 1991c). This reaction involves a one-electron transfer from the microsomal cytochrome P-450 system. Pentavalent chromium complexes are characterized as labile, reactive, and persistent; these characteristics make them likely candidates for interaction with cellular DNA (Jennette 1982).

Toxicity Values

Hexavalent chromium appears to exhibit no significant adverse systemic toxicity via ingestion. A 1-year drinking water study in rats showed no evidence of toxicity over the duration of the study (MacKenzie et al. 1958). The NOAEL for hexavalent chromium in the MacKenzie et al. (1958) study was calculated to be 0.003 mg/kg-day. EPA used an uncertainty factor of 300.

An oral Rfd of 0.003 mg/kg-day was established (EPA 1998). The dermal RfD was estimated by adjusting the oral RfD by 1% to get 0.00003 mg/kg-day (ATSDR 1993).

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p,p'-DDD, p,p= DDE, and p,p=DDT

Cancer

DDD, DDE and DDT is classified as a Category B2 probable human carcinogen on the basis of increased incidence of liver tumors including carcinomas in two strains of mice and in hamsters and of thyroid tumors in female rats exposed to DDE by diet (EPA 1995).

As reported by EPA (1995), human epidemiological data are not available for DDE. Evidence for the carcinogenicity in humans of DDT, a structural analog, is based on autopsy studies relating tissue levels of DDT to cancer incidence. These studies have yielded conflicting results. Three studies reported that tissue levels of DDT and DDE were higher in cancer victims than in those dying of other diseases (Casarett et al. 1968; Dacre and Jennings 1970; Wasserman et al., 1976). In other studies no such relationship was seen (Maier-Bode 1960; Robinson et al. 1965; Hoffman et al. 1967). Studies of volunteers and workers occupationally exposed to DDT have been of insufficient duration to determine the carcinogenicity of DDT to humans.

NCI (1978) administered DDE in feed at TWA doses of 148 and 261 ppm to 50 B6C3F1 mice/sex/dose for 78 weeks. After an additional 15 weeks, a dose-dependent and statistically significant increase in incidence of hepatocellular carcinomas was observed in males and females in comparison with controls. Increased weight loss and mortality was observed in females. Tomatis et al. (1974) administered 250 ppm DDE in feed for lifetime (130 weeks) to 60 CF-1 mice/sex. A statistically significant increase in incidence of hepatomas was observed in both males and females in comparison with controls. In females, 98% of the 55 surviving exposed animals developed hepatomas, compared to 1% of the surviving controls. Rossi et al. (1983) administered DDE in feed for 128 weeks to 40-46 Syrian Golden hamsters/sex/dose at doses of 500 and 1000 ppm. After 76 weeks, a statistically significant increase in incidence of neoplastic nodules of the liver were observed in both sexes in comparison with vehicle-treated controls.

NCI (1978) also fed DDE at TWA doses of 437 and 839 ppm for males and 242 and 462 ppm for females for 78 weeks to 50 Osborne-Mendel rats/sex/ dose, with an additional 35 week observation period. A dose-dependent trend in incidence of thyroid tumors was observed in females which was statistically significant by the Cochran Armitage trend test after adjustment for survival. The Fischer Exact test, however, was not statistically significant. Overall, the results of the bioassay were not considered by NCI to provide convincing evidence for carcinogenicity.

Mutagenicity

DDE was mutagenic in mouse lymphoma (L5178Y) cells and chinese hamster (V79) cells, but not in *Salmonella* (ICPEMC 1984).

Toxicity

Short term exposure to high doses of DDT, DDD and DDE primarily affects the nervous system. Studies indicate that exposure to DDT alters hepatic enzyme levels, but is not associated with toxicity in humans (ATSDR 1992).

Toxicokinetics

Oral exposure is considered the most significant route of exposure to DDT, DDD and DDE, but all are absorbed following inhalation, oral and dermal exposures (ATSDR 1992). Once absorbed, DDT, DDE and DDD are distributed to all body tissues and are stored there in proportion to organ tissue lipid content (Morgan and Roan 1971). Excretion of DDT and metabolites is largely via the urine, regardless of the route of exposure (ATSDR 1992).

Metabolism

The metabolism of DDT, DDE and DDD has been studied in humans and several mammalian species. In humans, metabolism of DDE is slow and DDE is retained in adipose tissues (Hayes et al. 1971; Morgan and Roan 1971).

Toxicity Values

EPA (1998) has estimated an oral slope factor for DDE and DDT of 3.4H10-1 $(mg/kg\text{-}day)^{-1}$ by applying the linearized multistage procedure, extra risk model to the tumor incidence data observed in three studies: NCI (1978), Tomatis et al. (1974), and Rossi et al. (1983). The oral quantitative estimate is a geometric mean of six slope factors computed from cited incidence data by sex. For comparison, the geometric mean obtained using the slope factors from the mouse studies alone is $7.8H10^{-1}$ (mg/kg-day), which is within a factor of 2 of that derived from the mouse and hamster studies combined. In addition, the slope factor for DDE was within a factor of 2 of the slope factors for liver tumors for three structurally similar compounds: DDT X $3.4H10^{-1}$ $(mg/kg\text{-}day)^{-1}$; DDD X $2.4H10^{-1}$ $(mg/kg\text{-}day)^{-1}$; and Dicofol X $4.4H10^{-1}$ $(mg/kg\text{-}day)^{-1}$. The carcinogenicity assessment for DDE is contained in EPA (1980) and EPA (1985).

Dermal slope factors were estimated by adjusting the oral SF by 100% to yield $3.4H10^{-1}$ $(mg/kg\text{-}day)^{-1}$ -DDT and $2.4H10^{-1}$ $(mg/kg\text{-}day)^{-1}$ for DDD (ATSDR 1993).

EPA established reference doses for health effects other than cancer for DDT of 0.005 mg/kg-day (USEPA 1998). For a dermal RfD, the oral RfD was used unaltered.

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DIBENZO(a,h)ANTHRACENE

Dibenzo(a,h)anthracene (DBA) ($C_{22}H_{14}$, MW 278.4, CAS registry number 53-79-3) is a polynuclear aromatic hydrocarbon described in its pure form as colorless plates or leaflets. It is insoluble in water, slightly soluble in alcohols, but soluble in most organic solvents such as benzene, toluene, and xylene. There is no commercial production or known use of DBA, and it occurs ubiquitously as a product of incomplete combustion, in fossil fuels, cigarette smoke, exhaust emissions from gasoline engines, coal tar, and edible oils.

Cancer

DBA is classified by EPA (1998) as a probable human carcinogen (Category B2), based on sufficient data from animal bioassays but no human data.

There were no studies found that investigated the carcinogenic effect of DBA in humans. DBA is a minor constituent in mixtures such as coal tar, soots, coke oven emissions, and cigarette smoke that have been associated with human cancer (IARC 1984).

DBA/2 mice (21/sex) were given an 0.2 mg/mL DBA in a water-olive oil emulsion for a total dose of 0.85 mg/day (males) and 0.76 mg/day (females) for 237B279 days (Snell and Stewart 1962, 1963). Treated mice developed pulmonary adenomas, pulmonary carcinomas, hemangioendotheliomas, and mammary carcinomas in females. Although no statistical analysis was reported, the incidences of tumors were significantly elevated relative to controls. In a gavage study, a single dose of 1.5 mg DBA in polyethylene glycol administered to Swiss mice produced forestomach papillomas after 30 weeks (Berenblum and Haran 1955).

DBA has produced positive results in mouse skin painting assays for carcinogenicity. Swiss mice developed carcinomas following dermal application of 0.001 percent DBA (Wynder and Hoffman 1959; Van Duuren et al. 1967). Studies demonstrating the complete carcinogenic activity and initiating activity of DBA are summarized in IARC (1973).

Subcutaneous (s.c.) injection of DBA has been demonstrated to produce injection site tumors in several species. Single s.c. injections of 2.4, 4.7, 9.3, 18.7, 37.5, or 75 µg DBA produced tumors that appeared to be dose-related (Pfeiffer 1977). Lubet et al. (1983) found that s.c. injections of DBA were associated with fibrosarcoma formation in specific strains of mice. C3H/HeH and C57B1/6 dosed with 150 mg DBA in 0.05 mL trioctanoin had higher incidences of tumor formation, but not in the AKR/J or DBA/2J mice that were also treated. The average latency period for fibrosarcomas varied with the strain and tended to be inversely correlated with the tumor incidence rate.

Mutagenicity

DBA was mutagenic to *S. typhimurium* (3B5 µg/plate) in the presence of exogenous metabolic system, *Escherichia coli* and *bacillus subtilis* (12B50 µg/well). DBA was mutagenic to mammalian cells, induced unscheduled DNA synthesis and sister chromatid exchange, and was positive in assays for morphological transformation (EPA 1995).

Toxicity

Acute intraperitoneal injection of 3B90 mg/kg bw DBA in sesame oil reduced the growth rate of young rats that persisted for at least 15 weeks (Haddow et al. 1937).
DBA administered by subcutaneous injection at a dose of 5 mg/rat from the onset of pregnancy resulted in fetal death and resorption and may have had adverse effects on subsequent fertility (Wolfe and Bryan 1939).

Toxicokinetics

DBA was applied to mouse skin at 1 µM/mouse and became bound to DNA in the treated area to the extent of 15 pmol/mg DNA (Phillips et al. 1979). DBA had a maximum level of binding 72 hours after treatment. DBA is biotransformed by the mixed function oxidase system to reactive intermediates that can bind to macromolecules such as DNA, leading to mutations and eventually cancer. The 5,6-oxide and the 1,2-, 3,4-, and 5,6-dihydrodiols have been detected as metabolites of DBA following incubation with exogenous activating system (Selkirk et al. 1971; NacNicoll et al. 1979; Nordqvist et al. 1979). The 3,4-dihydrodiol was active as a tumor initiating agent in mice (Buening et al. 1979; Slaga et al. 1980), and induced pulmonary tumors in newborn mice (Buening et al. 1979). The 3,4-dihydrodiol was the most mutagenic to bacteria (Wood et al. 1978).

The elimination of DBA and other PAHs has not been studied by any route in humans. The elimination of DBA has been studied after oral exposure in rats (Chang 1943). Approximately 90 percent of the DBA dose (not specified) was eliminated in the feces, and there was a dose-response

relationship between the administered DBA in the diet or by gavage and the percentage of hydrocarbon excreted in the feces.

Toxicity Values

The relative potency factor for BbF is 1.0 (EPA 1993). This toxicity equivalency factor is used in conjunction with the SF for benzo(a)pyrene (7.3 $(mg/kg\text{-}d)^{-1}$) to estimate cancer risks to DBA via oral exposures only. Inhalation and dermal cacner risks cannot be estimated for DBA (EPA 1993). No reference dose is available for DBA (EPA 1998).

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HEPTACHLOR EPOXIDE

Heptachlor epoxide is not commercially available in the United States, but is an oxidation product of the pesticide heptachlor.

Cancer

EPA (1998) has classified heptachlor epoxide as a Category B2 probable human carcinogen based on sufficient evidence from rodent studies in which liver carcinomas were induced in two strains of mice of both sexes and in CFN female rats. Several structurally related compounds are liver carcinogens.

Three epidemiologic studies of workers exposed to chlordane and/or heptachlor (Wang and McMahon 1979a,b; Ditraglia *et al*. 1981) exist. One retrospective cohort study showed marginal statistically significant increased mortality from bladder cancer (3 observed), but was considered inadequate in sample size and duration of follow-up (Wang and McMahon 1979a). Two other retrospective cohort studies were of pesticide manufacturing workers. Neither study showed any statistically significant increased cancer mortality (Wang and McMahon 1979b; Ditraglia *et al.* 1981), and both study populations also had confounding exposures from other chemicals.

Four long-term carcinogenesis animal bioassays of heptachlor epoxide have been reported (EPA 1995). The major finding in mice has been an increased incidence of liver carcinomas. Davis (1965) fed C3H mice 0 or 10 ppm heptachlor epoxide for 2 years. Survival was generally low, but a 2-fold increase in benign liver lesions (hepatic hyperplasia and benign tumors) over the controls was reported. Reevaluation by Reuber (1977) revealed a significant increase in liver carcinomas in the dosed group. Velsicol Chemical Co. (1973) tested a 75:25 mixture of heptachlor epoxide : heptachlor in CD-1 mice. The mice were fed 0, 1, 5, and 10 ppm for 18 months. A statistically significant increase of hyperplasia was observed in the 5 and 10 ppm dose groups in both sexes. Reuber=s reevaluation (EPA 1985) resulted in a change in diagnosis for benign to liver carcinomas, thereby increasing the incidence of hepatic carcinomas.

The earliest bioassay with rats (Witherup *et al.* 1955) tested CFN rats each at 0.5, 2.5, 5.0, 7.5, and 10 ppm for 108 weeks. The authors observed malignant and benign tumors randomly among test groups and controls. Reuber=s reevaluation (EPA 1985) reported a significant increase of hepatic carcinomas above the controls at 5 and 10 ppm in the female rats. A reevaluation by Williams (EPA 1985) reported a significant increase of hepatic nodules at the 10 ppm level in the males over the controls.

Mutagenicity

Gene mutation assays indicate that heptachlor epoxide is not mutagenic in bacteria (Moriya *et al.* 1983). In two mouse dominant lethal assays, heptachlor epoxide did not induce major chromosomal aberrations in male germinal cells (Arnold *et al.* 1977; Epstein *et al.* 1972). Ahmed *et al.* (1977) reported qualitative evidence of uuncheduled DNA synthesis response in SV40 transformed human fibroblasts in the presence of hepatic homogenates and heptachlor epoxide.

Toxicity

Chronic oral exposure to heptachlor or heptachlor epoxide effects the liver, with heptachlor effects also being observed for renal and neurological systems. Liver effects have included alterations in liver weights with minimal pathological influences on tissues. Kidney effects were altered weights, and an increase in blood urea (this may indicate kidney inefficiency in protein clearance). Neurological long-term effects may include tremors, muscle spasms, convulsions (ATSDR 1993).

In a chronic study (Dow Chemical Co. 1958), beagle dogs from 23 to 27 weeks of age were divided into five groups and given diets containing 0, 0.5, 2.5, 5 or 7.5 ppm of heptachlor epoxide for 60 weeks. Liver-to-body weight ratios were significantly increased in a treatment-related fashion. Effects were noted for both males and females at the lowest effect level of 0.5 ppm. A NOEL was not established (EPA 1995).

Toxicokinetics

Heptachlor epoxide is absorbed in the intestine, and tends to bioaccumulate in tissues with high fat contents. It segregates primarily into fat, and then into liver, kidney, and brain (ATSDR 1993).

Metabolism

Heptachlor epoxide is a natural degradation product of heptachlor, and is also the primary metabolite of heptachlor. Other metabolites or heptachlor epoxide have been observed, but it has a relatively long half-life (ATSDR 1993).

Toxicity Values

EPA (1998) has established an oral RfD for heptachlor expoxide of $1.3H10^{-5}$ mg/kg-d based on increased liver-to-body weight changes in dogs observed in a chronic feeding study (Dow Chemical Co. 1958). An uncertainty factor of 1000 was used to account for inter- and intra-species differences and to account for the fact that a NOEL was not attained (EPA 1998).

EPA (1998) has established an oral SF for heptachlor exposed of 7.3 $(mg/kg\text{-}d)^{-1}$.

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INDENO(1,2,3-cd)PYRENE

Indeno(1,2,3-cd)pyrene ($C_{22}H_{12}$, MW 276.3, CAS registry number 193-39-5) is a PAH that forms yellow plates or needles as a pure substance when recrystallized from light petroleum solution. Indeno(1,2,3-cd)pyrene is a product of incomplete combustion and also occurs in fossil fuels, cigarette smoke, exhaust emissions, and motor oils. It also is found in natural sources such as surface water. There is no commercial production of indeno(1,2,3-cd)pyrene.

Cancer

Indeno(1,2,3-cd)pyrene is considered by EPA to be a probable human carcinogen (Group B2) based on no human data and sufficient data from experimental animal studies (EPA 1998).

No studies have been located that investigated the carcinogenicity of indeno(1,2,3-cd)pyrene in humans. Indeno(1,2,3-cd)pyrene is a component of mixtures (e.g., coal tar, soots, coke oven emissions, and cigarette smoke) that have been associated with human cancer (EPa 1995).

Indeno(1,2,3-cd)pyrene has been shown to be an effective tumor initiating compound in mouse skin painting assays in several mouse strains (Hoffmann and Wynder 1966; Rice et al. 1986). Swiss albino Ha/ICR/Mil mice (20/group) dermally treated with indeno(1,2,3-cd)pyrene in acetone solutions (0.01, 0.05, and 0.1 percent) developed skin tumors (papillomas and carcinomas) in a dose-related manner (Hoffmann and Wyndner 1966). The authors also reported a total dose of 250 mg indeno(1,2,3-cd)pyrene applied in 10 applications in 2 days, followed by promotion with croton oil was a sufficient tumor initiating dose. Tumor incidence was essentially 100 percent in Crl:CD-1(ICR)BR female mice given a total initiating dose of 1 mg indeno(1,2,3-cd)pyrene in 10 days, followed by promoting agent TPA 10 days later (Rice et al. 1986).

Osborne-Mendel rats (35/group) received lung implants of indeno(1,2,3-cd)pyrene at doses of 0.65, 3.4, or 17 mg/kg in a 0.05 mL mixture of beeswax and trioctanoin for their lifetime (Deutsch-Wenzel et al. 1983). The incidence of epidermoid carcinomas in the lung and thorax was statistically significant and dose-related. The tumor occurrences were: 0 percent in untreated controls, 0 percent in vehicle controls, 11 percent in low-dose, 23 percent in mid-dose, and 60 percent in high-dosed animals.

Male and female CD-1 mice (32/group) were given intraperitoneal injections of indeno(1,2,3-cd)pyrene in DMSO on days 1, 8, and 15 after birth for a total dose of 580 µg/mouse (LaVoie et al. 1987). The animals were sacrificed at 52 weeks of age and evaluated for tumors. Only one male mouse developed a lung adenoma (not statistically significant), and no females developed tumors.

Mutagenicity

Indeno(1,2,3-cd)pyrene was mutagenic in *S. typhimurium* in strains TA100 and TA98 in the presence of an exogenous activating system (LaVoie et al. 1979; Hermann et al. 1980).

Toxicity

No studies have been found that investigated the developmental, reproductive, or any other toxicities of indeno(1,2,3-cd)pyrene in experimental animals.

Toxicokinetics

No studies were found on the toxicokinetics of indeno(1,2,3-cd)pyrene alone, although information about the toxicokinetics of PAHs as a class is discussed in the toxicity profiles for acenaphthene and benzo(a)pyrene above.

Toxicity Values

The relative potency factor for indeno(1,2,3-cd)pyrene is 0.1 (EPA 1993). This toxicity equivalency factor is used in conjunction with the SF for benzo(a)pyrene (7.3 $(mg/kg\text{-}d)^{-1}$) to estimate cancer risks to indeno(1,2,3-cd)pyrene via oral exposures only. Inhalation and dermal cacner risks cannot be estimated for indeno(1,2,3-cd)pyrene (EPA 1993). No reference dose is available for indeno(1,2,3-cd)pyrene (EPA 1998).

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IRON

Iron (Fe, CAS registry number 7439-89-6) is the fourth most abundant element in the earth=s crust and the second most abundant metal. It comprises approximately 5 percent of the continental crust. Its concentration in ground water ranges from 0.5 mg/L to 10 mg/L; its concentration in soil is between 0.7 and 4.2 percent (NRC 1979). In the late 1970s, world production of iron was over 500 million metric tons, with the U.S. producing roughly 20 percent of the world total (NRC 1979). Since iron is an essential nutrient, some amount of iron is needed in the diet.

Cancer

Iron has not been classified with respect to carcinogenicity, given the paucity of animal cancer bioassays and human cancer studies. Iron overload may be associated with carcinoma of the liver, however the data are poor and inconclusive (NRC 1979).

Mutagenicity

Iron has not been reported to be mutagenic (NRC 1979).

Toxicity

Acute Toxicity

The acute effects of iron toxicity in humans are well characterized and consist of gastrointestinal, cardiovascular, metabolic, neurological and hepatic alterations (Bothwell et al. 1979; Banner and Tong 1986; Engle et al. 1987; and Mann et al. 1989, all as cited in EPA 1993). Acute effects are based mostly on observations of children who accidentally ingest therapeutic iron supplements; they are rarely, if ever, associated with ingestion of naturally occurring or other commercially produced substances (NRC 1979). Gastrointestinal toxicity is characterized by vomiting, diarrhea, and abdominal pain, caused by the direct caustic effect of iron on the mucosa of the stomach and small intestine. Gastrointestinal toxicity can progress to gastric/intestinal hemorrhage and/or necrosis and, in rare cases, to stenosis in the stomach outlet and small intestine. Cardiovascular iron toxicity is marked by severe hemodynamic alterations and can lead to shock and cardiac failure; neurological toxicity ranges from lethargy to coma. Although a rare occurrence, hepatic toxicity from iron can range from cloudy swelling of hepatocytes to necrosis. The average human lethal dose is 200B250 mg/kg body weight (NRC 1979). Thus, the average adult male would have to ingest 14 grams of elemental iron for it to be lethal; the average 2 year old, 3 grams (NRC 1979).

General Toxicity

Chronic iron toxicity has been noted in individuals with various genetic and/or metabolic disorders, including hemochromatosis (massive iron overload together with cirrhosis and/or other tissue damage due to iron), thalassemia, and sideroblastic anemia, as well as in individuals who receive frequent blood transfusions (Jacobs 1977, and Bothwell et al. 1979, both as cited in EPA 1993). Excessive intake of iron attributed to consumption of home-brewed Kaffir beer has resulted in chronic hemochromatosis among the South African Bantu population (NRC 1979; and Bothwell and Bradlow 1960; and Bothwell et al. 1964, both as cited in EPA 1993). Pathologic findings associated with hemochromatosis include: 1) fibrosis in heavily siderotic organs, particularly the liver, 2) cirrhosis, 3) testicular atrophy, and 4) osteoporosis (NRC 1979).

Though chronic iron toxicity can occur in individuals with genetic/metabolic disorders, it is debatable whether a chronic overload via ingestion is possible in individuals with a normal ability to control iron absorption. Using values obtained from the second National Health and Nutrition Examination Survey (NHANES II), Looker et al. (1988, as cited in EPA 1993) compared dietary iron intake with biochemical indices of iron status. NHANES II consisted of a 1976B1980 sample of the U.S. population aged 6 months to 74 years. Observed intake levels of 0.15B0.27 mg/kg-day iron were found to be both great enough to prevent iron deficiency and insufficient to cause the toxic effects of iron overload (Elinder 1986; Cook 1991; Hillman and Finch 1985, all as cited in EPA 1993). Lauffer (1991, as cited in EPA 1993) and Sullivan (1992, as cited in EPA 1993) suggest that

iron overload elevates the risk of acute myocardial infarction by promoting oxidation of low density lipoprotein (LDL). A 1992 Finnish study of 1,931 randomly selected men aged 42B60 years by Salonen et al. lends support to this theory in that it found that high serum ferritin concentration and high dietary iron intake were risk factors for myocardial infarction.

Animal studies attempting to model hemochromatosis have been mostly negative, as have animal studies involving parenteral administration of iron (Bothwell et al. 1979, as cited in EPA 1993; and NRC 1979).

Reproductive/Developmental Toxicity

Ingestion of iron supplements during pregnancy has not been correlated to adverse developmental effects in humans, although some women ingesting large quantities of iron (>1.2 gram) during pregnancy experienced nausea, vomiting, hematoemesis, abdominal pain, and/or diarrhea (NAS 1989, as cited in EPA 1993). No teratogenic effects have been associated with iron (NRC 1979).

No treatment-related teratogenic or embryotoxic effects were observed in rats given 2.7 mg/kg-day iron on gestation days 6B15 or rats/mice given 24B76 mg/kg-day iron for 6 days (Nolen et al. 1972; Tadokoro et al. 1979, as cited in EPA 1993).

Toxicokinetics

This essential nutrient is found primarily in the form of hemoglobin in the body. The concentration of iron found in the body at any given point is regulated largely through changes in the amount of iron absorbed by the gastrointestinal mucosa. The following factors influence the absorption of iron: 1) body stores, 2) the amount and nature of iron in ingested food, and 3) dietary factors that may increase or decrease the availability of iron for absorption (NRC 1979). Although the body is generally effective in regulating iron levels, it is incapable of excreting large amounts of iron following excessive accumulation resulting from acute or chronic ingestion of high levels of iron (NAS 1989, as cited in EPA 1993).

Toxicity Values and Other Standards

Using values obtained from the second National Health and Nutrition Examination Survey (NHANES II), Looker et al. (1988, as cited in EPA 1993) compared dietary iron intake with biochemical indices of iron status. NHANES II consisted of a 1976B1980 sample of the U.S. population aged 6 months to 74 years. Observed intake levels of 0.15B0.27 mg/kg-day iron were found to be both great enough to prevent iron deficiency and insufficient to cause the toxic effects of iron overload (Elinder 1986; Cook 1991; and Hillman and Finch 1985, as cited in EPA 1993). EPA (1993) has proposed a provisional chronic oral RfD of 0.3 mg/kg-day based on a NOAEL of 0.27 mg/kg-day (i.e., the upperbound value in the range of mean dietary iron intakes from the NHANES II data base) and an uncertainty factor of 1. An uncertainty factor of 1 was used since: 1) iron is an essential nutrient, 2) the NHANES II data base comprised a relatively large sample size, and 3) humans exert an efficient homeostatic control over iron such that body burdens are kept

constant with variations in diet. EPA=s confidence in the critical study is high, while confidence in the data base is medium, resulting in medium confidence in the RfD. EPA (1993) suggests that the RfD may not be protective of people with inherited disorders of iron metabolism. In addition, EPA states that the RfD could be conservative if applied to exposure scenarios involving forms of iron with low bioavailability.

The NCEA has established a provisional chronic RfD of 0.3 (mg/kg/day). (EPA 1998)

Iron has not been classified with respect to carcinogenicity. SFs are not available for iron.

Other Standards

The TLV-TWA for iron salts is 1 mg/m^3 (ACGIH 1995).

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LEAD

Lead (Pb, MW 207.2, CAS registry number: 7439-92-1) is a bluish-gray metal which is malleable and possesses a relatively low melting point. Lead is produced commercially from ore obtained through mining. Lead is used commercially in the production of batteries, ammunition, and in a wide variety of metal products. Within the last several years, the use of lead in fuels, paints, and ceramics has been curtailed due to the increasing evidence of adverse health effects associated with lead exposure.

Cancer

The carcinogenicity of lead has been classified as Category B2 by the EPA (1998). No specific inhalation studies of cancer in animals or humans were located. There were no studies of cancer in humans following only oral exposure, although several epidemiological studies of occupationally exposed humans were conducted. Interpretation of these data is confounded by co-exposure to other potentially carcinogenic metals, as well as the inclusion of smokers in the studied populations. In several of these studies, small but statistically significant increases in either total malignancies (Kang et al. 1980; Cooper et al. 1985), digestive tract tumors (Kang et al. 1980; Cooper et al. 1985), or renal cancers (Selevan et al. 1985; Baker et al. 1980b) were observed.

Epidemiologic Data in Humans

Lead at very high doses has been shown to cause some tumors in animals (Azar et al. 1973; Koller et al. 1985; van Esch and Kroes 1969). However, epidemiological studies, despite large exposures among workers, have failed to indicate that lead may cause cancer in humans (Kang et al. 1980; Cooper et al. 1985; Selevan et al. 1985; Baker et al. 1980b). The EPA weight of evidence carcinogen classification of inorganic lead is B2 (i.e., a probable human carcinogen, based on animal evidence and minimal to no human data) for both oral and inhalation routes of exposure. However, no oral or inhalation slope factors are available for inorganic lead (EPA 1998).

Carcinogenicity Data in Animals

Animal studies have shown increased renal tumors in rat strains and one mouse strain after oral exposure to several soluble lead salts. Rats given lead acetate for 2 years developed renal tumors in a dose-dependent manner (Azar et al. 1973), while rats given a single dose

of lead acetate developed renal tubular carcinomas (Koller et al. 1985). Mice given lead acetate in the diet also showed increases in renal tumors (van Esch and Kroes 1969).

Mutagenicity

Lead acetate and lead chloride did not induce mutagenicity in *Salmonella*/microsome assays for base-pair and frame shift mutations, with or without microsomal activation (Rosenkranz and Poirier 1978; Simmon 1979; Simmon et al. 1979; Nestmann et al. 1979). There are conflicting reports on the effects of lead salts on mammalian chromosomes *in vitro* and *in vivo* (IARC 1980). Lead acetate induced cell transformation in Syrian hamster embryo cells (DiPaolo et al. 1978); however, no significant increases in structural chromosome aberrations or mitotic abnormalities were observed in Chinese hamster cells. Lead acetate has been reported to induce dominant lethal effects in mice in one study (Varma et al. 1974), but not in another study (Kennedy and Arnold 1971). Similarly, chromosomes from bone-marrow cells taken from mice fed for 2 weeks with lead acetate in the diet showed an excess of gaps and breaks (usually involving single chromatids) and of fragments (Muro and Goyer 1969). However, Jacquet et al. (1977) found no excess of severe chromosome or chromatid aberrations in bone-marrow cells of mice fed for 1B3 months with lead acetate in the diet. Factors that may influence i7nduction of chromosomal aberrations by lead include dose and nutritional status (Deknudt et al. 1977). Grandjean et al. (1983) showed a relationship between increased sister chromatid exchanges and lead exposure in workers.

Lead has been shown, in a number of DNA structure and function assays, to affect the molecular processes associated with the regulation of gene expression (EPA 1986).

Toxicity

The predominant systems effected by chronic (>365 days) lead inhalation or ingestion by humans are the hematological, neurological, and cardiovascular systems. Toxic hematological effects include inhibition of several enzymes involved in heme synthesis, with resultant depression of hemoglobin synthesis and anemia. Blood lead levels for these effects vary from having no threshold level (i.e., effects are seen at *any* blood lead level) for certain enzymes to 3B40 Φg/dL for others (Koren et al. 1990; Harlan et al.1988). The principal cardiovascular effect is elevation of blood pressure (Harlan 1988), a dose-dependent effect which also lacks any apparent threshold. Neurological effects typically manifest themselves as neurobehavioral effects and effects on the peripheral nervous system. Such effects can range from weakness in the limbs (Zimmerman-Tansella et al. 1983), fatigue (Hänninen et al. 1979; Baker et al. 1979), and loss of memory function (Haenninen et al. 1979), to significant impairment in learning capacity (Wang et al. 1989; Rummo et al. 1979; Ernhart et al. 1981), limb tremors (Baker et al. 1979), and encephalopathy at higher blood levels (Rummo et al. 1979). High levels of lead in the blood have also been correlated with nephropathy, gastrointestinal effects and electrocardiographic abnormalities (ATSDR 1993a).

No studies specifically related to effects from dermal exposure to inorganic lead were located. The dermal absorption of lead is estimated at less than 1 percent (i.e., 0.3 percent) (Moore et al. 1980).

If any amounts of lead were absorbed by this route, effects would be represented by the systemic effects described above for the other routes.

Toxicokinetics

Adult men absorbed approximately 10 percent of a radioactively labeled ingestion dose in studies by Rabinowitz et al. (1973 1976). In infants, a mean of 41.5 percent of ingested lead was observed in a study by Ziegler et al. (1978); individual absorption was related inversely to dietary calcium levels. Tissue distribution studies of lead in men fatally poisoned by tetraethyl lead revealed lead levels of 7B240 mg/kg present in tissues in the lung, brain, liver, and kidney (Davis et al. 1963). Low doses of an organic lead compound, tetraethyl lead, are distributed throughout various tissues, particularly to the brain. Tetraethyl lead breaks down into triethyl lead and minute amounts of inorganic lead, mainly in the liver; both products are excreted in the urine within a relatively short period of time (Tsuchiya 1979).

The majority of the effects of lead have been observed in occupationally exposed humans, where the routes of exposure are primarily inhalation and some oral ingestion of lead particulates. Effects of lead on humans are typically discussed in terms of their correlating absorbed internal body dose, a blood lead level (Φg/dL). In many instances, internal doses are actually the result of multiple routes of exposure. There does not seem to be a significant difference in the effects of lead via the inhalation versus the oral routes, and these effects will be discussed together. Dermal effects from inorganic lead exposure, the predominant form in soils, are minimal due to a negligible extent of dermal absorption.

Toxicity Values

An oral RfD for lead has not been derived by EPA (1998). Some health effects of lead may occur at blood lead concentrations so low as to be essentially without a biological threshold. This is the basis for EPA=s decision not to derive an RfD for lead. EPA=s Work Group discussed inorganic lead, and lead compounds, at two meetings (07/08/85 and 07/22/85) and considered it inappropriate to develop an RfD for inorganic lead (EPA 19985). In addition, an RfC has not been determined by EPA.

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MANGANESE

Cancer

EPA considers manganese to be unclassifiable as a human carcinogen (Category D), based on an absence of human carcinogenicity data, inadequate evidence of carcinogenicity in animals, and inadequate genotoxicity data (EPA 1998).

Mutagenicity

Few genotoxicity assays of manganese have been conducted. No studies were located regarding genotoxic effects in humans (ATSDR 1991). Treatment of male rats with manganese at repeated oral doses of 0.014 mg/kg-day manganese for 80 days did not produce any significant chromosomal damage in bone marrow or sperm cells (Dikshith and Chandra 1978). Results of *in vitro* genotoxicity assays have been mixed. The available data indicate that manganese may have genotoxic potential, but they are not sufficient to evaluate the genotoxic risk of manganese to humans (ATSDR 1991).

Toxicity

Humans exert an efficient homeostatic control over manganese such that body burdens are kept constant with variations in diet. Manganese is an essential element, being required for normal human growth and maintenance of health. Children may be less susceptible to manganese intoxication and may require slightly higher levels of manganese than do adults (EPA 1995).

The World Health Organization (WHO 1973) reviewed several investigations of adult diets and reported the average daily consumption of manganese to range from 2.0 to 8.8 mg/day. Higher manganese intakes are associated with diets high in whole-grain cereals, nuts, green leafy vegetables, and tea. Depending on individual diets, a normal intake may be well over 10 mg Mn/day, especially from a vegetarian diet. While the actual intake is higher, the bioavailability of manganese from a vegetarian diet is lower, thereby decreasing the actual absorbed dose. From manganese balance studies, the WHO concluded that 2B3 mg/day is adequate for adults and that 8B9 mg/day is Aperfectly safe≅ (WHO 1973).

The Food and Nutrition Board of the National Research Council (NRC 1989) determined an Aadequate and safe≅ intake of manganese to be 2B5 mg/day for adults. This level was chosen because it includes an Aextra margin of safety≅ from the level of 10 mg/day, which the NRC considered to be safe for an occasional intake.

The information used to determine the RfD for manganese in food was taken from many large populations consuming normal diets over an extended period of time with no adverse health effects (WHO 1973; NRC 1989; Schroeder et al. 1966). A NOAEL of 0.14 mg/kg-day (corresponding to 10 mg/day for a 70 kg adult) is based on a composite of data from all three references.

An epidemiologic study of manganese in drinking water was performed by Kondakis et al. (1989). Three areas in northwest Greece were chosen for this study, with manganese concentrations in natural well water of 3.6B14.6 µg/L in area A, 81.6B252.6 µg/L in area B, and 1,600B2,300 µg/L in area C. The total population of the 3 areas being studied ranged from 3,200 to 4,350 people. Although the amount of manganese in the diet was not reported, the authors indicated that most of the food was purchased from markets. The individuals chosen were submitted to a neurologic examination, the score of which represents a composite of the presence and severity of 33 symptoms (e.g., weakness/fatigue, gait disturbances, tremors, dystonia). Whole blood and hair manganese concentrations were also determined. The authors indicate that the difference in mean scores for area C versus A was significantly increased for both sexes combined. In a subsequent analysis, logistic regression indicated that there is a significant difference between areas A and C, even when both age and sex are taken into account (Kondakis 1990). The NOAEL identified in this epidemiological study was 0.005 mg/kg-day (EPA 1995).

The major toxic effects of inhaled manganese are primarily neurological. A syndrome called Amanganism≅ has been observed only in workers exposed to chronic, high levels of manganese. It is characterized by preliminary general weakness, anorexia and muscle pain, with psychological signs such as apathy and dullness, as well as impotence. Advanced stages include difficulty in walking, muscle tremor, and behavioral disturbances. This syndrome has not been observed for low level, chronic or sporadic exposures, nor has it been observed in studies with animals (ATSDR 1991).

Roels et al. (1992) conducted a cross-sectional study of 92 male workers exposed to manganese dioxide (MnO_2) dust in a Belgian alkaline battery plant. A control group of 101 male workers was matched for age, height, weight, work schedule, coffee and alcohol consumption, and smoking; educational level was slightly higher in the control group. The manganese-exposed group had been exposed to MnO_2 for an average of 5.3 years (range: 0.2B17.7 years). The geometric means of the workers= TWA airborne manganese concentrations, as determined by personal sampler monitoring at the breathing zone, were 0.215 mg/m^3 for respirable dust and 0.948 mg/m^3 for total dust. The authors noted that the personal monitoring data were representative of the usual exposure of the workers because work practices had not changed during the last 15 years of the operation of the plant.

Geometric mean concentrations of blood manganese (MnB) (0.81 µg/dL) and urinary manganese (MnU) (0.84 µg/g creatinine) were significantly higher in the Mn-exposed group than in the control group, but on an individual basis no significant correlation was found between either MnB or MnU and various external exposure parameters. A self-administered questionnaire focused on occupational and medical history, neurological complaints, and respiratory symptoms. Responses to the questionnaire indicated no significant differences between groups in either respiratory or neurological symptoms, nor were spirometric, hormonal, or calcium metabolism measurements significantly different for the two groups (Roels et al 1992).

Of particular note, manganese workers performed worse than controls on several measures of neurobehavioral function. Visual reaction time was consistently and significantly slower in the manganese-exposed workers measured in four 2-minute periods, with more pronounced slowing over the total 8-minute period and significantly greater variability in reaction times for the exposed group. Abnormal values for mean reaction times (defined as greater than or equal to the 95th percentile of the control group) also were significantly more prevalent in the exposed group during three of four 2-minute intervals of the 8-minute testing period. Five measures of eye-hand coordination (precision, percent precision, imprecision, percent imprecision, and uncertainty) reflected more erratic control of fine hand-forearm movement in the exposed group than in the controls, with mean scores on all five measures being highly significantly different for the two groups. There was also a significantly greater prevalence of abnormal values for these five measures in the manganese-exposed group. The hole tremormeter test of hand steadiness indicated a consistently greater amount of tremor in the exposed workers, with performance for two of the five hole sizes showing statistically significant impairment (Roels et al. 1992).

A LOAEL may be derived from the Roels et al. (1992) study by using the IRD concentration of MnO_2, expressed as mg/m^{3}Hyears (based on 8-hour TWA occupational exposures for various job classifications, multiplied by individual work histories in years). Dividing the geometric mean IRD concentration (0.793 mg/m^{3}Hyears) by the average duration of the workers= exposure to MnO_2 (5.3 years) yields a LOAEL of 0.15 mg/m^3. Adjusted for continuous exposure, the LOAEL is 0.05 mg/m^3.

Roels et al. (1987) conducted a cross-sectional study in 141 male workers exposed to MnO_2, manganese tetroxide (Mn_3O_4), and various manganese salts (sulfate, carbonate, and nitrate). A matched group of 104 male workers was selected as a control group. The two groups were matched for socioeconomic status and background environmental factors; in addition, both groups had comparable work-load and work-shift characteristics. Significant differences in mean scores between manganese-exposed and reference subjects were found for objective measures of visual reaction time, eye-hand coordination, hand steadiness, and audio-verbal short-term memory. The prevalence of abnormal scores on eye-hand coordination and hand steadiness tests showed a dose-response relationship with blood manganese levels; short-term memory scores were related to years of manganese exposure but not to blood manganese levels. The prevalence of subjective symptoms was greater in the exposed group than in controls for 20 of 25 items on the questionnaire, with four items being statistically significant: fatigue, tinnitus, trembling of fingers, and irritability. Based upon the findings of impaired neurobehavioral function in workers whose average Mn exposure was estimated by the geometric mean TWA of total airborne manganese dust at the time of the study, a LOAEL of 0.97 mg/m^3 was identified, which, when adjusted for continuous exposure, is equivalent to a LOAEL of 0.34 mg/m^3. This LOAELis based on total manganese dust of mixed forms, whereas the LOAEL from Roels et al. (1992) study is based on the measured respirable dust fraction of MnO_2 only.

Minimal information regarding manganese and the dermal exposure route could be located. It is generally regarded that manganese uptake across intact skin is very limited, as is the case for most inorganic forms of metal ions (ATSDR 1991).

Toxicokinetics

Exposure to manganese mainly occurs via ingestion and inhalation. The extent to which manganese is absorbed across the intestine is approximated at 3B5 percent, and does not appear to be substantially influenced by the carrier medium (i.e., water versus food). Similar extents of absorption have been noted in animals as well, with typical amounts equal to 2.5B5.5 percent. Manganese distributes to various tissues following ingestion, and serves as a normal tissue constituent. Tissue levels may be somewhat higher in animal tissues than in their human tissue counterparts. Manganese which is inhaled, typically in particle form, is absorbed to some unknown extent across the lungs, and a certain percentage of inhaled manganese particles are subsequently swallowed and ingested as well (ATSDR 1991).

Metabolism

Manganese is not known to be metabolized or biotransformed, and behavior within the body would be essentially limited to absorption, distribution, potential sequestration, and excretion. The valence state of manganese is thought to undergo changes within the body (alterations in oxidation state), which may influence its ability to form complexes or serve as a co-factor for certain proteins (ATSDR 1991).

Toxicity Values

Two separate oral RfDs for manganese have been established by the EPA: one based on ingestion of manganese in water and the other based on the ingestion of manganese in food (EPA 1998). The Food and Nutrition Board of the National Research Council (NRC 1989) determined an Aadequate and safe≅ intake of manganese to be 2B5 mg/day for adults. This level was chosen because it includes an Aextra margin of safety≅ from the level of 10 mg/day, which the NRC considered to be safe for an occasional intake. An RfD of $5H10^{-3}$ mg/kg-day for manganese in water is equivalent to a drinking water standard of 0.2 mg/L and is based on human chronic ingestion data (Kondakis et al. 1989). The RfD for ingestion of food is $1.4H10^{-1}$ mg/kg-day and is also based on a NOAEL derived from human chronic ingestion data (NRC 1989; WHO 1973; Schroeder et al. 1966). Because these RfDs are based on NOAELs identified in chronic human studies, no uncertainty factors were applied in calculating them (EPA 1998). EPA has assigned these chronic RfDs as surrogates for use with subchronic exposures without adjustment (EPA 1994).

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MERCURY

Inorganic mercury (Hg, CAS registry number 7439-97-6) is a ubiquitous metallic element and one of the most widely studied toxicants.

Cancer

At present, EPA considers mercury to be unclassifiable as a human carcinogen (Category D), based on an absence of human carcinogenicity data, inadequate evidence of carcinogenicity in animals, and inadequate genotoxicity data (EPA 1998).

Evidence for carcinogenicity in humans is considered inadequate by EPA (1998). Mortality studies were conducted workers exposed to elemental mercury vapors. Data showed conflicting results between the correlation of mercury exposure and increased carcinogenicity.

Animal carcinogenicity studies are briefly summarized by EPA (1998):

> When 39 rats were injected *i.p.* over 2 weeks with metallic mercury and observed for their lifetimes, sarcomas were seen only in those tissues that had been in direct contact with the metal (Druckrey et al. 1957). No concurrent controls were reported.
>
> The relevance of data from studies of organic mercury to the possible carcinogenicity of inorganic mercury is uncertain.

Genotoxicity

Limited evidence has shown that exposure to mercury can cause adverse affects in the number or structure of chromosomes. In a comparison of 4 men exposed to mercury vapor and unexposed controls, the exposed group shoed statistically increase in incidence of chromosomal aberrations in white blood cells (Popescu et al. 1979). Mabille et al. 1984, studied the chromosomal structure of occupationally exposed workers to mercury and did not find any significant increases in structural aberrations.

Toxicity

Ingestion is one of the primary routes of exposure to mercury, but elemental mercury is only very poorly absorbed from the gastrointestinal tract (probably less than 0.01 percent) (Hammond and Beliles 1980). While CNS effects are the typical target organ effects observed following inhalation exposures, renal effects are the primary target of ingested inorganic mercury. In chronic exposures, nephrotoxicity is typically manifest as proteinuria; in severe cases, the nephrotic syndrome is observed, with subsequent edema and hypoproteinemia (Hammond and Beliles 1980).

The major toxic effects of inhaled mercury are primarily neurological. In acute exposure scenarios, clinical signs include paresthesia, ataxia, dysarthria, and deafness (Berlin 1979). Chronic exposure typically involves exposure to both mercury vapor and divalent mercury. Toxic symptoms include renal damage with nephrotic syndrome as well as increased salivation, inflammatory changes of the gums and the appearance of black lines along the gums (Skerfving and Vostal 1972).

In historical medicinal preparations, treatment with mercury compounds produced skin reactions such as erythema and dermatitis (Bhamra and Costa 1992). Other clinical signs include irritation,

desquamation, loss of hair, ulcerations, hyperplasia and hyperkeratosis (Bhamra and Costa 1992; Matheson et al. 1980).

Toxicokinetics

Exposure to mercury mainly occurs via inhalation and ingestion. Absorption of mercury from the respiratory and gastrointestinal tracts is dependent on its chemic form (Berlin 1979). Mercury vapor is very efficiently absorbed from the lungs, while elemental mercury is poorly absorbed from the gut (Bhamra and Costa 1992). After gastrointestinal absorption, elemental mercury is oxidized to a divalent form which accumulates mainly in the kidney and in part in the lung. Divalent mercury does not traverse the blood brain barrier as readily as mercury vapor. Inorganic mercury will also accumulate in the intestinal tract, skin, spleen, and testes, but to lesser degrees (Bhamra and Costa 1992). Elimination of mercury vapor is primarily by exhalation, with an estimated biological half-time of approximately 60 days (Hurst et al. 1976; Rohala et al. 1973), while mercury sequestered in the brain may take several years for a halving of retained mercury (Rossi et al. 1976). Divalent mercury, with an estimated biological half-time of 42 days, is primarily excreted in the urine and feces (Rohala et al. 1973).

Metabolism

Inorganic mercury is not known to be metabolized or biotransformed, and behavior within the body would be essentially limited to absorption, distribution, potential sequestration, and excretion.

Toxicity Values

The oral RfD for mercuric chloride, is 1 H 10^{-4} mg/kg-day. This is based on a rat subchronic feeding and subcutaneous studies (EPA 1987) and autoimmune effects. The Uncertainty factor of 1000 is based on 10 for LOAEL to NOAEL conversion, 10 for use of subchronic studies, and a combined 1- for both animal to human and sensitive human population (EPA 1998).

EPA has not determined an oral SF (EPA 1998).

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VANADIUM

Vanadium (V; Chemical Abstracts Service [CAS] registry number 7440-66-6) is an elemental metal used primarily as an alloying agent in metals; other uses include industrial catalytic functions, in pesticides, dyes and pigments, and other uses. While functional roles for vanadium in higher organisms have yet to be confirmed, recent evidence supports the concept that vanadium is an essential micronutrient for animals (French and Jones 1992).

Cancer

No studies were located by ATSDR (1990d) during the agency's review of the toxicological literature regarding the carcinogenic effects of vanadium or vanadium compounds in humans or animals. As reported by the International Agency for Research on Cancer (Boffetta 1993), there is negative experimental studies for carcinogenicity of metallic vanadium, vanadyl ions, and trivalent vanadium 2,4-pentanedione. No data on humans exposed to vanadium and its compounds are available (Gilman and Swierenga 1984). Leonard and Gerber (1994) similarly noted the lack of data for a carcinogenic determination, but mentioned that vanadium is mitogenic with the concomitant potential for associated carcinogenicity (e.g., Ames and Gold 1990).

Mutagenicity

Vanadium or vanadium compounds are generally positive in bacterial (Kada et al. 1980; Kanematsu et al. 1980), yeast (Sora et al. 1986), rodent (Smith 1983), and human cell (Birnboim 1988; Hanauske et al. 1987) *in vitro* genotoxicity assays. However, there are no in vivo assays which have assessed the genotoxicity of vanadium compounds (as reported by ATSDR 1990d). In a recent summary, Leonard and Gerber (1994) conclude that vanadium compounds are not clastogenic, but can be weakly mutagenic.

Toxicity

Exposures to vanadium compounds occur largely through the food (for the general populace), while industrial workers are more commonly exposed to vanadium-containing dusts, fumes, and aerosols.

Ingestion exposures to vanadium compounds produces a variety of systemic and other effects. In humans, study volunteers were fed capsules containing 0.47B1.3 mg V (as ammonium vanadyl tartrate) per kilogram body weight for a duration of 3 months. Subjects reported intestinal cramping and diarrhea, but no effects to the hematological, hepatic, or renal systems (Dimond et al. 1963); however, concurrent experimental controls were lacking, and effects are not necessarily directly attributable to vanadium (ATSDR 1990d). Rodent mortality (LD_{50}) occurred at doses of approximately 30B40 mg V (as $NaVO_3$) kg^{-1} (Llobet and Domingo 1984), but chronic dietary exposures at 4.1 mg V (as $VOSO_4$) were not lethal (Schroeder and Balassa 1967; Schroeder et al. 1970). A three-month exposure to NaVO3 in drinking water produced

mononuclear cell infiltration in rat lungs, primarily in the perivascular region (Domingo et al. 1985), and cardiovascular effects in rodents are also reported (Susic and Kentera 1986). Major effects in humans of inhalation exposures to vanadium are irritant in nature, as observed from a variety of occupational epidemiological studies, case reports, and clinical studies; in general, irritation to the respiratory tract occurs at lower concentrations than do signs of skin or eye irritation (Calabrese and Kenyon 1991). Exposure of male white rats (n=11 per exposure group) to a 70-day-duration continuous fumigation with 0, 0.002, or 0.27 mg V (as V_2O_5) m^{-3} produced a suite of significant systemic effects in the high-exposure group that were not observed in the low-exposure group (Pazynich 1966). Effects included alterations in motor chronaxy, decreased oxyhemoglobin content, effects to leukocyte nuclei, and pathological conditions in several organ systems (lungs, liver, kidneys, and heart). The ATSDR (1990d) summarizes a variety of inhalation exposure studies, but present quantitative exposure information for only acute studies; sub-chronic or chronic studies were apparently lacking in detail to provide the agency with quantitative toxicological information, and what effects are presented therein are only cursorily discussed.

The effects of dermal exposure to vanadium or vanadium compounds appear largely unstudied. Dermal absorption and skin irritation were reported following application of a 20 percent solution of sodium metavanadate was applied to rabbit skin (Stokinger 1967); human skin absorption, however, may be very low (EPA 1977), as evidenced by a lack of skin penetration during an *in vitro* study using radiolabelled vanadium (Roshchin et al. 1980).

Toxicokinetics

Vanadium is absorbed from a variety of foods with a relatively low efficiency, but in sufficient quantities to be stored at detectable levels in many body tissue (French and Jones 1992). Gastrointestinal absorption generally ranges at less than 5 percent of the ingested dose (Byrne and Kosta 1978; Curran et al. 1959; Nielsen 1994), while airborne vanadium is absorbed very efficiently by the lungs (Boyd and Kustin 1985). The ICRP (1960) indicated that approximately 25 percent of soluble vanadium compounds may be absorbed via the respiratory tract. Although the body burden of vanadium is typically very small (French and Jones 1992), the element distributes throughout the body with a preferrential accumulation usually observed in the liver, kidney, and bone (Byrne and Kosta 1978; Nechay et al. 1986; Mongold et al 1990). Blood is the medium for the distribution of vanadium, of which about 95 percent of the vanadium is bound to transferrin as the vanadyl ion (V^{+4} as VO^{+2}) (Patterson et al. 1986). Because of the low level of absorption via the gastrointestinal tract, the majority of ingested vanadium is excreted via the feces; absorbed vanadium is excreted primarily through the kidneys in the urine (WHO 1988)

Metabolism

As an elemental molecule, vanadium *per se* is unmetabolizable, however, metabolic incorporations of vanadium have been studied. In the biological tissues, vanadium occurs largely as interconversions between two oxidation states: tetravalent vanadyl (V^{+4}) or pentavalent vanadate (V^{+5}) (ATSDR 1990d). Within the organism, the role of vanadium has yet to be

definitively understood, although a suite of generalized effects occur under conditions of vanadium deficiency. As summarized by French and Jones (1992), effects of vanadium deficiency include: increased abortion and perinatal death rates, decrease milk production, hepatic lipid and phospholipid changes, growth impairment (of bone, tooth, and cartilage), nutritional edema, thyroid metabolism changes, and depressed overall growth. Although poorly understood and of widely-varying types, the pharmacological actions of vanadium are receiving increasing recent attention, particularly with respect to insulinomimetic properties (as summarized by French and Jones 1992).

Toxicity Values:

The oral RfD for vanadium is 710^{-3} (mg/kg-day) (EPA 1998) with an uncertainty factor of 100. The cancer slope factor has not determined. The dermal RfD was estimated using an adjustment factor of 2%, on the oral slope factor (ATSDR 1992). The dermal RfD was estimated to be 0.0001 mg/kg-day.

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ZINC

Zinc (Zn) is an ubiquitous, nutritionally-essential trace element that also plays various industrial roles in galvanizing processes, paint formulations, and rubber, glass, or paper production. Zn provides a protective coating on other metals as it does not rust, and it is also used in alloys such as bronze and brass to make electrical equipment, zinc and copper to make U.S. coins. Zinc salts are used in ceramics, textiles, batteries, and also in the pharmaceutical industry as a solubilizing agent in many drugs. Zinc is found in the environment and in all foods and is released into the environment from anthropogenic activities such as mining, purification of Zn, steel production, and burning of coal and wastes. Zinc is an essential element required by humans in small amounts, but is deleterious to health in too little or too great quantities.

Toxicity

The toxic effects observed in humans following oral exposure to zinc as zinc oxide included abdominal pain, vomiting, anemia (ATSDR 1992), decreased HDL cholesterol (Chandra 1984; Hooper et al. 1980), and pancreatic damage (Chobanian 1981; Murphy 1970) at a dose greater than 10 times the recommended dietary allowance for zinc. High doses of Zn in humans cause decreased levels of hemoglobin and hematocrit, and similar effects were observed in other experimental animals species (ATSDR 1992). Ulceration of the forestomach and intestinal bleeding were reported for mice dosed with 1,110 mg Zn/kg-day and ferrets dosed with 390 mg/kg-day (Maita et al. 1981, Straube et al. 1980).

As a dietary requirement, oral exposure to zinc has been well-studied in animals and humans. With a variety of experimental durations (from >14 days to >1 year), adverse effects from zinc excess include mortality, gastrointestinal, hematological, musculo-skeletal, hepatic, renal, immunological, and developmental changes (ATSDR 1992). In general, most of the animal NOAELS for these effects occur at daily ingestion of zinc ranging from 10 to 100 mg/kg, although dog NOAELs of 2 mg/kg-day for gastrointestinal and musculo-skeletal toxicity were obtained by Anderson and Danylchuk (1979) in a 9-month study of dogs given zinc in drinking water. For the same types of adverse effects, the typical range of human LOAELs and NOAELs range from 1 to 5 mg/kg-day, although Kynast and Saling (1986) reports a NOAEL of 0.09 mg/lg-day for developmental effects in humans administered daily doses of zinc aspartate in capsules for 11 weeks duration.

Toxicity Values

EPA has established an oral reference dose (RfD) of 0.3 mg zinc (as a soluble salt) ingested per kilogram body weight per day, based on a decrease in erythrocytic superoxide dismutase content in adult human females after 10 weeks of zinc exposure (Yadrick et al. 1989). This RfDis based upon a dietary supplement LOAEL dosage of approximately 60 mg/kg, converted to 1 mg/kg-day, and by applying an aggregate uncertainty factor of 3. The uncertainty factor accounts for the use of a minimal LOAEL from a moderate-duration study of the most sensitive humans and consideration of a substance that is an essential dietary nutrient (EPA 1998).

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APPENDIX C: STREAMLINED HUMAN HEALTH RISK ASSESSMENT PROTOCOL

STREAMLINED HUMAN HEALTH RISK ASSESSMENT

The following steps are proposed as the methodology which will satisfy the requirement to perform a Streamlined Human Health Risk Assessment (SHHRA) for the former Naval Training Center-Bainbridge (NTC-B).

1.a. For each Area of Concern (AOC), e.g., the pesticide shop, the highest detected value of each potential contaminant among all samples will be screened against EPA Region III's latest Risk Based Concentration (RBC) for that contaminant in residential soils

b. The highest detected value will be used for screening even if the data carries a validation qualifier such as "J = estimated value"; the exception to use of qualified data will be "R = data not usable based on Quality Control".

c. Each contaminant which exceeds the RBC for carcinogenic effects or ten percent (10%) of the RBC for non-carcinogenic effects will be carried forward for further evaluation as a Contaminant of Potential Concern (COPC).

2. For each COPC, the set of all data points, other than R-qualified results, will be evaluated using the Shapiro Wilkes test to determine whether that data set is Normal, or log-Normal. The 95% UCL (upper confidence limit) will be computed for the data set, as appropriate for Normal or log-Normal data.

For purposes of computing the 95% UCL: Each sample point which is a Non-detect (U-qualified data) will be loaded into the computation as one-half the detection limit, and B-qualified data (same contaminant was also detected in the sample blank) will be considered to be one-half of the reported value.

3. The 95% UCL for each COPC will be input into the following algorithms (equations) as the soil concentration, C, and the cancer and non-cancer risks will be estimated for adult resident and child resident receptors subjected to both oral and dermal exposures.

The Absorption Factor, ABS, is chemical specific for the dermal pathways, and values will be taken from EPA Region III technical guidance Assessing Dermal Exposure for Soil, EPA/903-K-95-003, December 1995. Reference Doses (RFD) and Cancer Slope Factors (CSF) will be taken from IRIS.

4. The Cancer Risks (CR) and Hazard Quotients (HQ) arising from each COPC will be summed across pathways for each receptor. If any receptor exceeds a HQ greater than 1.0 or a CR greater than 1.0-E4, the site will be addressed in terms of Risk Management approaches.

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SOIL EXPOSURE - ORAL / INGESTION

SITE: _____
RECEPTOR: _____

EQUATIONS:

D= (C x IR x EF x ED x Fi x ABS x CF) / (BW x AT)

D=INGESTED DOSE (MG/KG/DAY)
C= CONCENTRATION IN SOIL (MG/KG)
IR= SOIL INGESTION RATE (MG/DAY)
EF= EXPOSURE FREQUENCY (DAYS/YR)
ED= EXPOSURE DURATION (YRS)
Fi= FRACTION INGESTED FROM SOURCE
ABS= ABSORPTION FRACTION
CF= CONVERSION FACTOR (KG SOIL/MG SOIL: 1E-6)
BW = BODY WEIGHT (KG)
AT = AVERAGING TIME (DAYS); -C = CANCEROUS, OR -NC = NON-CANCER

HQ = D / RFD

HQ = HAZARD QUOTIENT
RFD = REFERENCE DOSE (MG/KG/DAY)

CR = 1 - EXP(-CSF x D)

CR = CANCER RISK
CSF = CANCER SLOPE FACTOR

INPUTS		ADULT RESIDENT	CHILD RESIDENT
IR	_____	100	200
EF	_____	350	350
ED	_____	24	6
Fi	_____	1	1
ABS	_____	1	1
BW	_____	70	15
AT-NC	_____	8760	2190
AT-C	_____	25550	25550

SOIL EXPOSURE - DERMAL

EQUATIONS:

D= (C x SA x ABS x AF x EF x ED x CF) / (BW x AT)

D = DERMAL DOSE (MG/KG/DAY)
C= CONCENTRATION IN SOIL (MG/KG)
SA = SKIN AREA AVAILABLE FOR CONTACT (CM2/DAY)
ABS = ABSORPTION FRACTION
AF = SOIL-TO-SKIN ADHERENCE FACTOR (MG/CM2)
EF = EXPOSURE FREQUENCY (DAYS/YR)
ED = EXPOSURE DURATION (YRS)
BW = BODY WEIGHT (KG)
AT = AVERAGING TIME (DAYS); -C = CANCER, OR -NC = NON-CANCER
CF = CONVERSION FACTOR (KG SOIL/MG SOIL: 1E-6)

HQ = D / RFD

HQ = HAZARD QUOTIENT
RFD = REFERENCE DOSE (MG/KG/DAY)

CR = 1 - EXP(-CSF x D)

CR = CANCER RISK
CSF = CANCER SLOPE FACTOR

INPUTS		ADULT RESIDENT	CHILD RESIDENT
SA	_____	3000	1800
AF	_____	0.03	0.2
EF	_____	350	350
ED	_____	24	6
BW	_____	70	15
AT-NC	_____	8760	2190
AT-C	_____	25550	25550

APPENDIX -D: SUMMARY OF SOIL BACKGROUND DATA, NAVAL TRAINING CENTER -BAINBRIDGE

SOIL BACKGROUND DATA, NAVAL TRAINING CENTER - BAINBRIDGE

ANALYTE	8-SS-1	8-SS-2	8-SS-3	8-SS-4	8-SS-5	8-SS-6	8-SS-7	8-SS-8
ALUMINUM	11400	7950	13400*	17300*	3270	17700	11600	5450
ANTIMONY	0.18UL	0.27UL	0.23UL	0.21UL	0.18UL	0.19UL	0.17UL	0.5J
ARSENIC	10.7	4.4	6*	4.6*	2.1	4.4	5.6	7.8
BARIUM	29.7*	140*	82.2	78.2	9.1*	83.9*	18.6*	33.3*
BERYLLIUM	0.45B	0.58B	0.66	0.74	0.1U	0.99	0.19B	0.15B
CADMIUM	0.23U	0.79B	0.25B	0.17B	0.23U	0.25U	0.22U	0.29U
CALCIUM	496J	21500J	3730J	2530J	74.1JB	233J	44.4JB	928J
CHROMIUM	11.7*	9.2*	11.2*	16.1*	4.1*	13*	21.7*	10.7*
COBALT	4.3	4.3	7.1	7.8	0.99B	8.4	1.7B	1.7B
COPPER	32.3	17	20.4J	13.1J	1.7B	11.8	6.6	18.9
IRON	12300	6500	19900	16700	4120	25400	17500	14000
LEAD	98.6J	40.6J	38J	58.1J	10000J	23.5J	22J	61.5J
MAGNESIUM	2030	2980	2270*	3560*	196	3690	369	421
MANGANESE	143*	764*	551J	450J	11.9*	344*	33.2*	55.9*
MERCURY	0.11	0.68	0.16	0.1	0.14	0.05	0.1	0.15
NICKEL	5.9	7.8	7.5	9	1.8B	11.6	4.8	5.7
POTASSIUM	952	1280	642J	1560J	302	1060	261	368
SELENIUM	0.4B	0.45B	0.83B	0.63B	0.22U	0.4B	0.25B	1.1B
SILVER	0.42U	0.63U	0.54U	0.49U	0.42U	0.46U	0.4U	0.52U
SODIUM	33.1B	35.4B	58.8	47.8	15.6B	20.5B	13.7B	19.9B
THALLIUM	0.34U	0.51U	0.43U	0.4U	0.34U	0.37U	0.32U	0.63B
VANADIUM	22.3	15.4	47.4	32.1	11.2	45.4	35.6	28.8
ZINC	45.8	79.6	62.3	64.6	8.8	60	13.9	42.2

U = Not Detected

J = Estimated

L = Reported value may be biased low

B = Between IDL and CRDL

* = Duplicate analysis outside control limits

April 1999

RESPONSE TO COMMENTS ON THE DRAFT STREAMLINED HUMAN HEALTH RISK ASSESSMENT AOC 2,3, AND 6 NAVAL TRAINING CENTER - BAINBRIDGE

REVIEWER: Jennifer Hubbard, U.S. EPA Region III

Comment:

1. Section 2.0: The report should include a sample-location map. The report should also include the full set of validated data, probably as an appendix.

Response:

Brief site histories, sample location maps and site data tables will be presented in the Final Streamlined Human Health Risk Assessment. In addition, the validated background data will be included as an appendix.

Comment:

2. In the background database, a lead detection of 10,000 mg/kg (in sample 8-SS-5) was reported in the background data set. Because this concentration is highly unusual, especially for background soil, this should be double-checked. There may have been a paperwork error in reporting this result, or this may not be a suitable background lead location due to the presence of another source.

Response:

The lead detection of 10,000 mg/kg in Sample 8-SS-5 has been re-examined and it is a valid data point. A field duplicate taken at this same location was measured between 4,000 and 5,000 mg/kg (duplicate was eliminated from the risk assessment because both datapoints were valid and the 10,000 mg/kg concentration was higher). It is understood that these levels are not representative of background, therefore this sample point will not be used for this purpose. The remaining seven background soil samples will be used to represent background lead levels. (The Navy is preparing to conduct additional sampling in the area surrounding the 8-SS-5 sample location noted above to evaluate this abnormality.)

Comment:

3. In Section 2.0,3rd sentence, the meaning of one "additional" groundwater sample is not clear.

Response:

The word additional will bc removed from the text for clarification. The text will state that one ground-water sample was taken.

Comment:

4. Section 2.0 should identify what the samples were analyzed for. According to the data I received, AOC 2 consisted of 15 samples for PAHs and metals; AOC 3 consisted of 14 samples for pesticides; 8 background samples were analyzed for metals only; and at AOC 6, a single groundwater sample was analyzed for VOCs.

Response:

As noted earlier, the Final Streamlined Human Health Risk Assessment will include a history of site use for AOCs 2, 3, and 6, **as** well as detail numbers of samples, location of samples, and what analytes were assessed in these samples.

Comment:

5. Section 2.0, Selection of COPCs, 2nd paragraph: The statement about essential nutrients specifies four, **not** five; iron should be deleted. (Iron should have been evaluated for AOC 2.)

Response:

Iron will be removed from the list of essential nutrients in Section 2.0. and addressed as other elements with respect to COPC screening.

Comment:

6. Section 2.0, Surface Soil COPCs; and Table 1.4: For AOC 2, iron should be added as a COPC; naphthalene does not need to be a COPC. For AOC 3, chlordane could be evaluated as the combination of alpha-chlordane, gamma-chlordane, and heptachlor epoxide; or as total chlordane only. This review considers both methods. (Total chlordane was reportedly quantified using the alpha-chlordane, gamma-chlordane, and heptachlor expoxide peaks, therefore one could use the total chlordane result and **omit the** other chemicals, to eliminate double-counting; or one could use the individual compound results and omit total chlordane. This report used the latter approach. To compare the methods, my review demonstrates the risks using both methods.)

Response:

Iron will be added as a COPC at **AOC** 2 and screened against 1/10th of the Region III RBC of

23,000 mg/kg. Naphthalene, which was inadvertently identified as a COPC in Table 1 .1 and carried through the streamlined risk assessment process, will he removed as a COPC from AOC 3. As discussed during the Conference call of 10 February 1999 with the USEPA, Navy and EA, risks for technical chlordane will be examined as individual chemicals (alpha and gamma chlordane, heptachlor, and heptachlor epoxide).

Comment:

7. Section 3.0, Estimating Exposure Point Concentrations: The report should indicate the acceptance level (alpha) used during the Wilk-Shapiro test. Lognormality of the data was confirmed.

Response:

The report will indicate that the acceptance level used during the Wilk Shapiro test (a =0.05)

Comment:

8. Table 1 .1: The screening value for chromium should be 23 mg/kg. The screening value for mercury, if based on the more conservative methyl mercury, would be 0.78 mg/kg Iron should be a COPC. The screening value for naphthalene should be 160000 ugikg, but this chemical is still below the screening level (BSL) and need not be a COPC.

Response:

The chromium screening value used (1/10th of the May 1997 RBC of 390 mg/kg) will be modified to reflect 1/10th of the most current RBC of 230 mg/kg Other screening values will be modified as appropriate to reflect any other changes in Region III residential RBCs. While it is true that the methyl mercury screening value would be lower at 0.78, it would not affect the outcome of the screening process (mercury would still be a COPC regardless of the form of mercury). In addition the use of divalent mercury (as mercuric chloride) for the representative form of mercury is more appropriate for soil than methyl mercury. Consequently, the screening value for mercury (2.3 mg/kg will remain unchanged. As noted in the response to Comment 6, iron will be included as a COPC and naphthalene will be removed as a COPC.

Comment:

9. Table 1.2: For total chlordane, the screening level would be 1800 ug/kg

Response:

As noted in the response to Comment 6, it was decided to quantify chlordane risks on the basis of the individual chlordane isomers rather than technical chlordane. Therefore, thhe focus of the

human health risk assessment will remain on alpha and gamma chlordane as well as heptachlor epoxide.

Comment:

10. Table 1.3 is not really necessary, since all chemicals were not detected. For this reason, the screening toxicity values were not checked on this table.

Response:

Concur. Table 1.3 will be removed from the streamlined human health risk assessment. Because the document is now a stand alone document, and a chapter has been added which describes the three sites, samples taken at these sites, and the data from these samples it is no longer necessary to have Table l-3 in the human health risk assessment.

Comment:

11. Table 2.1: Iron should be added, with a lognormal UCL of 59560 mg/kg. For antimony, if the B-flagged result for 2-SS-9 is omitted, **the UCL becomes 7X mg/kg** and the maximum of 71 mg/kg would be the exposure point concentration. The maximum concentration of dibenz[a,h]anthracene appears to be 0.47 rather than 0.45 mg/kg. Napthalene is not necessary

Response:

As noted earlier, iron will be considered a COPC in the revised streamlined human health risk assessment.

The validator "B" qualified concentration of 1 m&g for 2-SS-9 represents that this concentration is within 5X of the associated blank contamination. In lieu of deleting this data, the 1 .O mgikg concentration be considered as a detection limit, and included in the 95 % UCL calculation at 1/2 the detection limit.

The value of 0.45 mgikg as the maximum detected concentration for dibenz[a,h]anthracene is correct. The 0.47mg/kgvalue is reported, however it represents the detection limit for that sample and does not qualify as a detected concentration

As noted in the response to Comment 6, naphthalene was inadvertently included as a COPC, and will be eliminated in the document revision.

Comment:

12. Table 2.2: The UCL for total chlordane would be 103.2 mg/kg.

Kesponse:

As noted in the response to Comment 6, chlordane risks will be addressed and quantified for the detected components of chlordane; cis and trans chlordane and heptachlorcpoxidc.

Comment:

13. Page 4, Exposure Population and Pathways, 1st paragraph: Adults are typically assumed to he exposed for 30 years. However, if one considers part of that as a childhood lifetime segment, the adult portion is 24 years. The adult noncancer exposure could be calculated for 30 years, but since exposure duration cancels out for noncancer exposure, an adult's HI at 24 years would equal the HI at 30 years.

Response:

The draft document dated November 1998 indicated the wrong exposure times, however, the draft document of December 1998 showed the proper duration of 6 and 24 years for children and adults respectively. Risk calculations were all performed using the proper exposure duration.

C o m m e n t :

14. Page 4, Exposure Population and Pathways: The RME is not intended to represent the worst-case scenario. RME is reasonable maximum exposure, which is a high-end, but not an upper-bound or worst-case, scenario.

Response:

The text regarding the definition of RME will be changed from "The reasonable maximum exposure (RME) is intended to represent the worst case scenario for the above cited exposure pathways." To "The reasonable maximum exposure (RME) is intended to represent the highest exposure that is reasonably expected to occur at the site."

Comment:

15. Page 5: The lead level of 10 ug/dL is sclcctcd as the level below which any potential effects are expected to be very subtle, given that no threshold has yet been identified for lead. The report should also mention that EPA's goal is that no more than 5% of exposed children should exceed this level.

Response:

The text will also include the EPA's goal that no more than 5% of the exposed children should

exceed the 10 ug/dL blood lead level.

Comment:

16. Table 3.1: The Region IV dermal guidance should not have been used for this Region III assessment. The following dermal slope factors are recommended (in units per mg/kg/day), based on chemical-specific adjustment factors: arsenic, 1.5 (adjustment factor 95%, NCEA 1992); DDD, 0.24 (adjustment factor 80 to 100% ATSDR 1993); DDE and DDT, 0.34 (adjustment factor 80 to l00%, ATSDR 1993); chlordanes, 0.4 (adjustment factor 80%, ATSDR 1994). Lead has been classified as a Group B2 carcinogen, but without a slope factor.

Response:

The risk assessment will be revised and the Region III dermal guidance note above will be used in the HHRA.

Comment:

17. Table 3.2: The Region IV dermal guidance should not have been used for this Region III assessment. The following dermal reference doses are recommended (in units of mg/kg/day based on chemical-specific adjustment factors: antimony, 4E-5 (adjustment factor 10% ATSDR 1992); arsenic, 3E-4 (adjustment factor 95%, NCEA 1992); barium, 7E-2 (adjustment factor l00%, NCEA 1993); cadmium 2.5E-5 (adjustment factors 5% from water RfD and 2.5% from food RfD IRIS); chromium, 3E-5 (adjustment factor I%, ATSDR 1993); manganese, 2E-2 (adjustment factor assumed to be 100% for non-food sources); mercury, lE-4 for methyl and 3E-4 for inorganic (adjustment factor 100%; IRIS and ATSDR 1997); vanadium, IE-4 (adjustment factor 2%, ATSDR 1992); DDT, 5E-4 (adjustment factor 80 to l00%, ATSDR 1993); chlordanes, 4E-4 (adjustment factor 80%, ATSDR 1994); naphthalene. 2E-2 (adjustment factor 80%, ATSDR 1993).

Iron should **be** added, with oral and dermal RfDs of 0.3 mg/kg/day and target organs of blood, liver and GI system (NCEA 1996, confirmed 1999). The aluminum neurotoxicity is developmental. The arsenic oral RfD is 3E-4 mg/kg/day The first organ likely to be affected for chromium is the kidney. The oral RfD for manganese is 2E-2 (for non-food sources). The target organ for manganese is the central nervous system. The methyl mercury RfD is IE-4 m&g/day. For methyl mercury, the target organ is developmental neurotoxicity; for inorganic mercury, the target organ is the immune system. For vanadmm, the HEAST vanadium number should be used (7E-3 mg/kg/day no identified target organs).

Response:

Reference to Region IV guidance will be removed from the document, and the dermal reference doses and other RfDs referenced above will he used in the recalculation of risks for the chemicals noted.

Comment:

18. Section 5.0: At the beginning of each section, where it states, "Chronic health effects other than cancer were estimated .", this should read "Chronic hazard indices for health effects other than cancer were estimated ."

Response:

The sentence will be amended to reflect the above wording.

Comment:

19. Section 5.0, AOC 2; Section 7.0; and Tables 4.1 and 4.2: My risk estimates were similar to those in the report. However, because of the iron COPC and some issues with respect to exposure point concentration and dermal toxicity factors, there were some differences, I estimated a child HI of 10, due mainly to iron (2.6), antimony (2.7), arsenic (1.3), chromium (0.6), manganese (0.8), and mercury (0.9). I estimated a total cancer risk of lE-4 (lE-4 for child and 4.5E-5 for adult), which was driven by benzo[a]pyrene and arsenic. For adults, the HI was approximately 1.4, but the driving chemicals did not share target organs (antimony, 0.4; arsenic, 0.2; chromium, 0.2; iron, 0.3; mercury, 0.1).

To determine whether the risk-driving metals were site-related, a student t test was used to compare background and on-site data (after natural log transformation). (Benzo[a]pyrene could not be tested because background samples were analyzed for metals only.) At a 5% acceptance level, only antimony exceeded background levels. However, the high detection of arsenic (74 mg/kg) exceeded the 95% UCL on the 95th percentile of the background data set (the upper tolerance limit, 24 mgikg), suggesting that this detection may be a hot spot. Therefore, the report's focus on arsenic and antimony seems appropriate, although benzo[a]pyrenc should be discussed also.

Response:

These comments have been noted. Risk calculations will be rerun using all input parameters noted in Comments 16 and 17, iron will be included as a COPC, and new risks presented in the final document

Comment:

20. Section 5.0, AOC 2, Adult Residents: Instead of stating that there are no noncancer risks

to adult residents, this should state that there are no unacceptable noncancer risks to adults.

Response:

The final report will reflect that no unacceptable noncancer risks were found to affect adult residents.

Comment:

21. Section 5.0, AOC 3; Section 7.0; and Tables 4.1 and 4.2: For the original chorodane scenario (considering all the components individually), I estimated a child HI of 4 (which would be 5 under the alternate scenario of total chlordane). The DDT HQ was 1.8, with an original chlordane HI (sum of heptachlor epoxide, alpha-chlordane, and gamma-chlordane) of 0.8 + 0.5 + 0.4 = 1.7 or an alternate chlordane HI of 3.2. For the cancer risk, I estimated 7E-5 (original) or 9E-5 (alternate) for the child, 4E-5 (original) or 6E-5 (alternate) for the adult, with a total of lE-4 (original) to 1.5E-4 (alternate). For the adult HI, I estimated a total of 0.5 (original) or 0.8 (alternate).

It is apparent that there is fairly good correlation between the original and alternate methods of chlordane quantitation. The total chlordane is probably slightly more conservative because it includes other peaks, such as nonachlor, that were not individually quantitated.

Response:

This comment has been noted. As noted earlier, chlordane risks will be quantified using individual chlordane components

Comment:

22. Section 5.0, AOC 3, Adult Residents: Instead of stating that there are no noncancer risks to adult residents. this should state that there are no unacceptable noncancer risks to adults.

Response:

The final report will reflect that no unacceptable noncancer risks were found to affect adult residents.

Comment:

23. Section 5.1 states that the maximum lead concentration was used in the IEUBK model.

In this model, the average should be used. It is also not clear what dust value was used in the equation.

Response:

The final report will use the average lead concentration in the IEUBK model and the dust value (70% of lead found in soil, the default value) will be noted in the report.

Comment:

24. Page 8, top; and Figure 1: At the maximum soil concentration (3950 mg/kg), with the multisource dust model, I generated a geometric mean of 16.4 ug/dL with 83.75% above 10 ug/dL. This does not quite match Figure 1. (However, the mean should be used rather than the maximum.) Using the mean of 530 mgikg with the multisource dust model, the geometric mean is 6.1 ug/dL, with 13.64% above 10 ug/dL. Using the UCL of 1969 mg/kg with the multisource dust model, the geometric mean is 15 ug/dL, with 78.4% above 10 ug/dL. In any case, lead does appear to be a potential concern at AOC 2.

Response:

This comment has been noted and the lead model will be rerun using the mean concentration rather than the maximum concentration.

Comment:

25. Section 7.0 should also contain a summary of the lead information for AOC 2.

Response:

A summary of blood lead levels will be included in Section 7.0.

Comment:

26. Section 8.0, AOC 2: With the antimony concentration of 71 mg/kg and the HI of 2.7, the PRG would be 26 mg/kg not vastly different from 32 mg/kg.

It should be noted that the cancer risk at the arsenic non-cancer PRG would be 6E-5.

With the arsenic cancer risk of 7.6E 5, the cancer PRG would be 0.4 mg/kg which in not vastly different from 0.27 mg/kg. For benzo[a]pyrene (concentration 4.3 mg/kg, cancer risk 5E-5), the cancer PRG at lE-6 would be 0.09 mg/kg.

It should be noted that setting the arsenic cancer risk at lE-4 would correspond to an

exceedance of the non-cancer PRG; the benzo[a]pyrene risk should also be considered.

Response:

These comments have been noted. As indicated earlier risks will bc recaclulated and presented in the final document.

Comment:

27. Section 8.0, AOC 3: The weighting of the target HIs should be explained.

With the following HQs, the noncancer PRGs were derived as follows: DDT (HQ 1.8): A 3 mg/kg alpha-chlordane (HQ 0.4): 4.3 mg/kg; gamma-chlordane (HQ 0.5): 4.4 mg/kg; heptachlor epoxide (HQ 0.75): 0.5. These are not greatly different from the noncancer PRGs in the report.

The cancer PRGs for the original chlordane approach were verified, except for heptachlor epoxide. A cancer risk of 1.3E-5, not 3.6E-5, was generated. Therefore, the PRG at lE-6 would be 0.05 mg/kg; at lE-5 would be 0.5 mg/kg and at 1.6E-5 would he 0.8 mg/kg.

If the alternate method were used for total chlordane, then the PRG at a cancer risk of lE-6 would be 1.3 mg/kg (and the total cancer risk would bc lower than 6E-6), and at an HI of 0.87 (assuming DDT would remain at 0.13) the PRG would be 28 mg/kg.

Response:

The weighting of target HIs will be explained in the final report.

The reviewer is correct that the correct cancer risk for heptachlor epoxide was 1.3E-5, not 3.6E-5 as shown in the draft report. Resultant PRGs based on this level of risk are correct as shown in the comment. However, Comments 16 and 17 have modified several exposure factors which will change the baseline risk from heptachlor epoxide (as well as all other chemicals). The Final Streamlined Human Health Risk Assessment will reflect these newly calculated baseline risks as well as PRGs derived from the risks.

Comment!

28. It should be noted that the risk-based PRGs should be applied as means (lead) or upper confidence limits on the mean (other chemicals)

Response:

The text will be revised to note that during risk-based PRG application appropriate concentrations to consider are the mean for lead and the upper confidence limit for other

chemicals.

Comment:

23. Appendix A: The Region III guidance for VOC dcrmal absorption from soil is 0. 05% to 3% for non-occluded skin. However, this report did not address soil VOCs, so there were no effects on the quantitative risk estimates.

Response:

Comment noted.

Comment:

30. Appendix B: The numerical factors in these profiles should be adjusted in accordance with previous comments (16 and 17).

Response:

The factors will be adjusted as per Comments 16 and 17.

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